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CARDIOLOGY

OFFICIAL JOURNAL OF THE American College of Cardiology

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Symposium on Pericarditis

ELWYN EVANS, M.D., F.A.C.C.
Guest Editor

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JANUARY 1961

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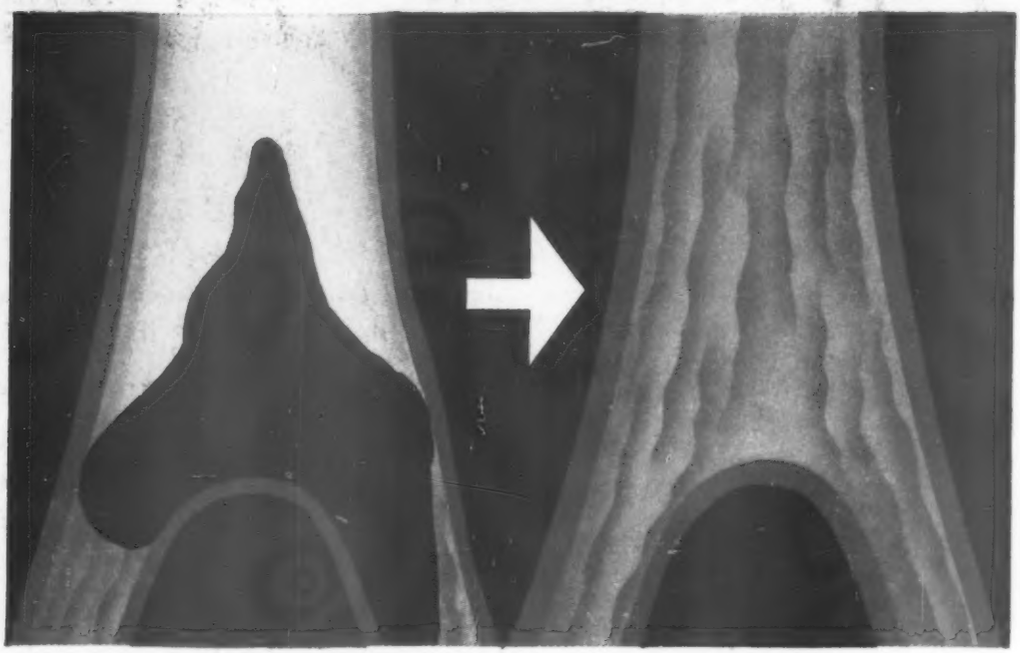

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*Klass, A.: Cur. Therap. Res. 2:322 (July) 1960.

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References: **1.** Tandowsky, R. M.: Personal communication. **2.** Parsons, W. B.: *Curr. Therapeut. Res. 2*:137 (May) 1960. **3.** Thompson, C. E.: Personal communication. **4.** Biben, L. H.; Kurstin, W., and Protas, M.: Personal communication. **5.** Hobbs, T. G.: Personal communication.

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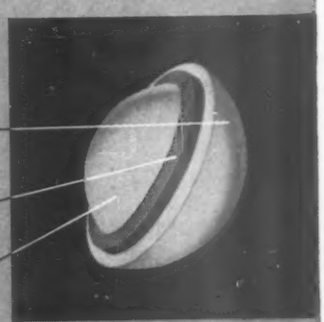

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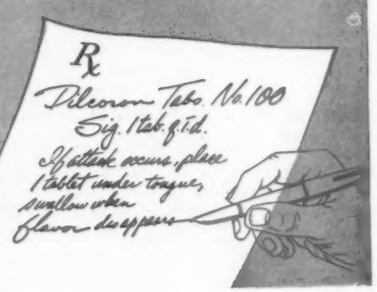

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ELWYN EVANS

Pericarditis: A Ten Year Survey 7
DANIEL C. CONNOLLY AND HOWARD B. BURCHELL

Experience at the Mayo Clinic with acute nonspecific pericarditis suggests a virus etiology with an associated autoimmune process is responsible for this frequently benign condition. Not to be overlooked are such complications as pericardial effusion with tamponade, hemorrhage, acute relapses, chronic constrictive pericarditis and myocarditis. Adrenal steroid therapy may help but steroid dependence and hypercorticoadrenalism may prove disturbing complications.

Auscultatory Findings in Diseases of the Pericardium 15
W. PROCTOR HARVEY

The characteristic friction rub of pericarditis is composed of three parts which occupy presystole, systole and diastole. "Pericardial knock" may be heard in early diastole in patients with constrictive pericarditis.

The Electrocardiogram in Pericarditis 21
EDGAR HULL

The electrocardiogram in many cases of significant pericardial disease shows characteristic abnormalities such as elevation of RS-T junction, T wave changes and low voltage.

Roentgenography of Pericardial Disease 33
ISRAEL STEINBERG

The clues to the diagnosis of the various forms of pericardial disease are excellently demonstrated in this review. Angiocardiography establishes the diagnosis of pericardial effusion and aids in corroborating the diagnosis of pericardial constriction and intrapericardial tumors. It also differentiates pericardial disease from enlargement of the heart and great vessels and from mediastinal tumors.

Chronic Constrictive Pericarditis 48
PAUL WOOD

Re-emphasizing the major features of constrictive pericarditis and its treatment, this comprehensive article describes the more significant refinements in the knowledge of this subject acquired during the past ten to fifteen years.

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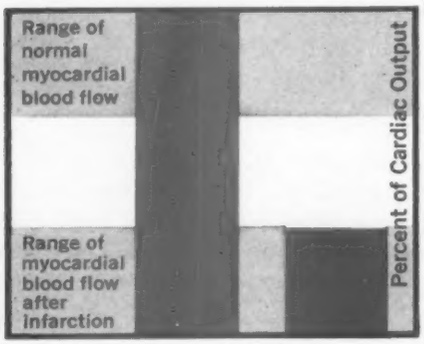
confirmed by radioisotopic measurements
in coronary artery disease

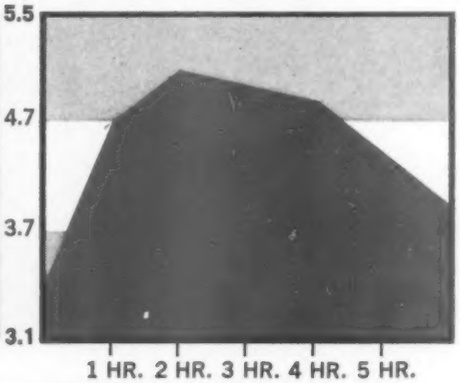
*Peritrate produces "significant" and "prolonged" increase in myocardial blood flow**

MYOCARDIAL BLOOD FLOW IN NORMAL AND POSTCORONARY PATIENTS



There is a significant reduction in myocardial blood flow in patients with a previous myocardial infarction.

EFFECTS OF PERITRATE ON POSTCORONARY PATIENTS



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*Johnson, P. C., and Sevelius, G.:
Measurement of myocardial blood flow, J.A.M.A. *173*:1231 (July 16) 1960.

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Chronic Constrictive Pericarditis Treated with Pericardiectomy 62
DONALD B. EFFLER

Surgical experience with twenty-six patients operated upon at the Cleveland Clinic Hospital for chronic constrictive pericarditis reveals successful decortication depends on an adequate surgical exposure and favorable pericardial condition. Myocardial disease and postoperative complications produce a less favorable outcome.

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The Postpericardiotomy Syndrome 73
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Postpericardiotomy Syndrome Following Traumatic Hemopericardium 83
BERNARD TABATZNIK AND JAMES P. ISAACS

Seventy-eight per cent of fifty survivors of traumatic hemopericardium recovered within two or three weeks; 22 per cent had recurrent pericardial and pleural effusion and other complications. From this it is adduced that the postcommissurotomy syndrome results from surgical trauma, not from rheumatic activation.

Traumatic Pericarditis 97
R. W. KISSANE AND STEWART M. ROSE

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Hemopericardium without trauma was found in 105 of 21,000 autopsies at the Los Angeles County Hospital due to myocardial infarction (60 per cent), aortic aneurysms (33 per cent), metastatic carcinoma (4 per cent) and blood dyscrasias (3 per cent).

Pericarditis in Children 109
ALEXANDER S. NADAS AND JAY M. LEVY

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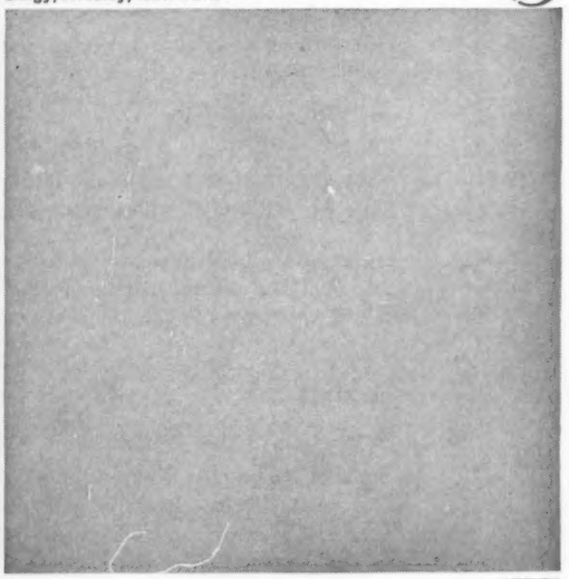

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ERNEST W. CROW

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Within two years a blunt chest injury produced cardiac tamponade and constrictive pericarditis which surgery relieved completely.

Diagnostic Shelf

Effect of Respiration on the Pericardial Friction Rub 130
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"What shall it profit us all if we gain the whole world of science and lose our collective souls"?

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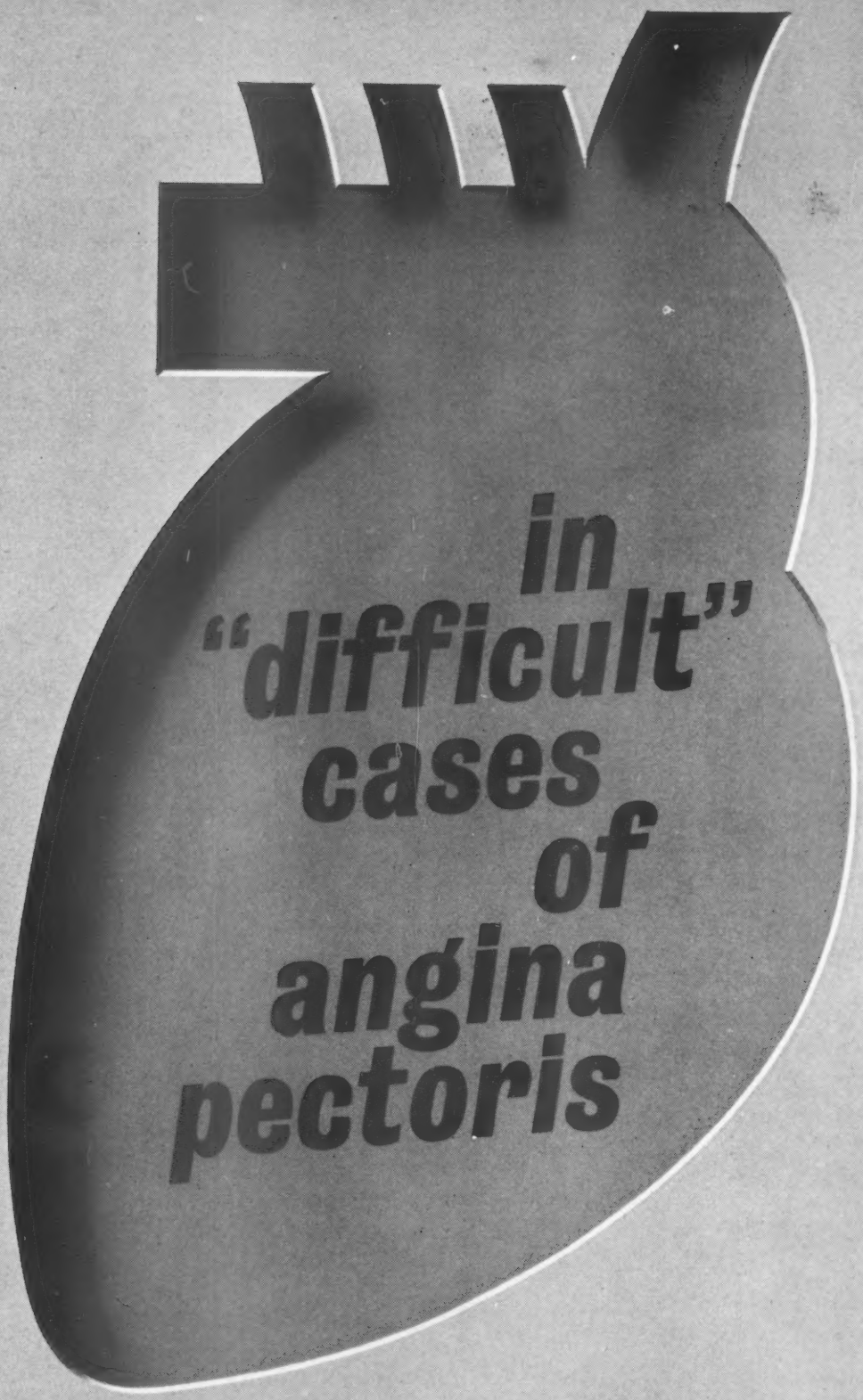

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References: 1. W. Hollander and R. W. Wilkins, in J. H. Moyer, Ed., Hypertension, Philadelphia, W. B. Saunders Co., 1959, p. 399. 2. R. W. Oblath, paper read at American Therapeutic Society, 60th Annual Meeting, Atlantic City, N. J., June 6, 1959. 3. N. Bloom, **Virginia M. Month.**, 87:23, 1960. 4. T. Winsor and P. Zarco, **Angiology**, 11: (Part 2), 67, 1960. 5. G. C. Griffith, **Clin. Med.**, 6:1555, 1959. 6. G. C. Griffith, **Dis. Nerv. System**, 21 (Suppl.), 101, 1960.

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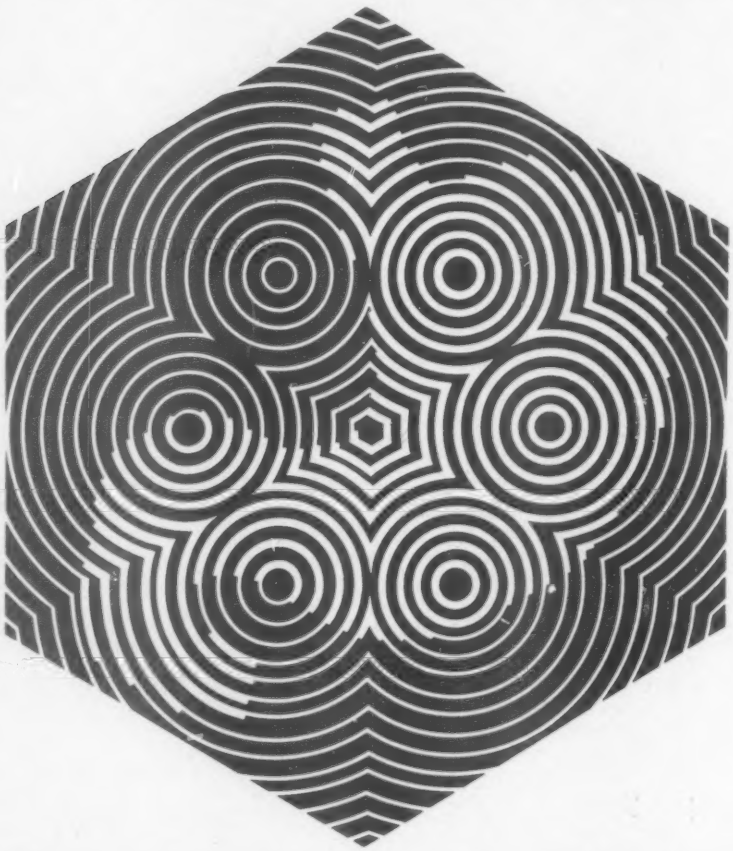

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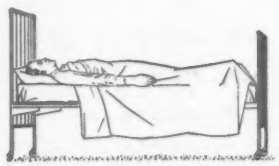
Effect on duration of illness and convalescence[1]		Weeks of hospitalization or bed rest at home are commonly required in the management of thrombophlebitis, phlebothrombosis, pulmonary embolism, and arterial thrombosis.
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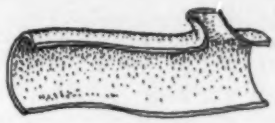
Anticoagulants cannot remove formed clot. However, they may help prevent its extension and may minimize formation of new clots.	 Recently formed intravascular clots are usually lysed rapidly and the formation of new clots may be inhibited. Circulation is usually restored and maintained, with rapid symptomatic relief.
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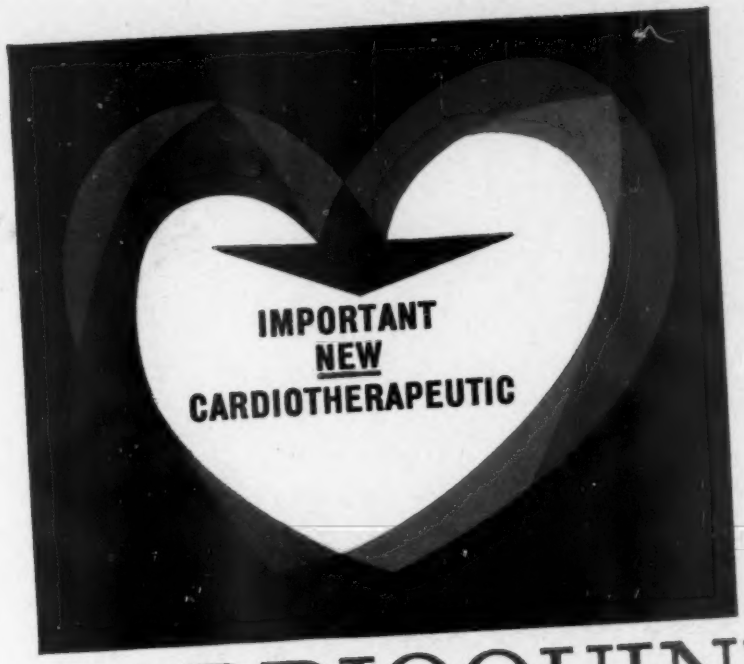

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2. Russek, H.I.: Circulation *18*:774 (Oct.) 1958.

3. Hirshleifer, I., *et al.*: Scientific Exhibit, A.M.A., Atlantic City, N. J., June, 1959.

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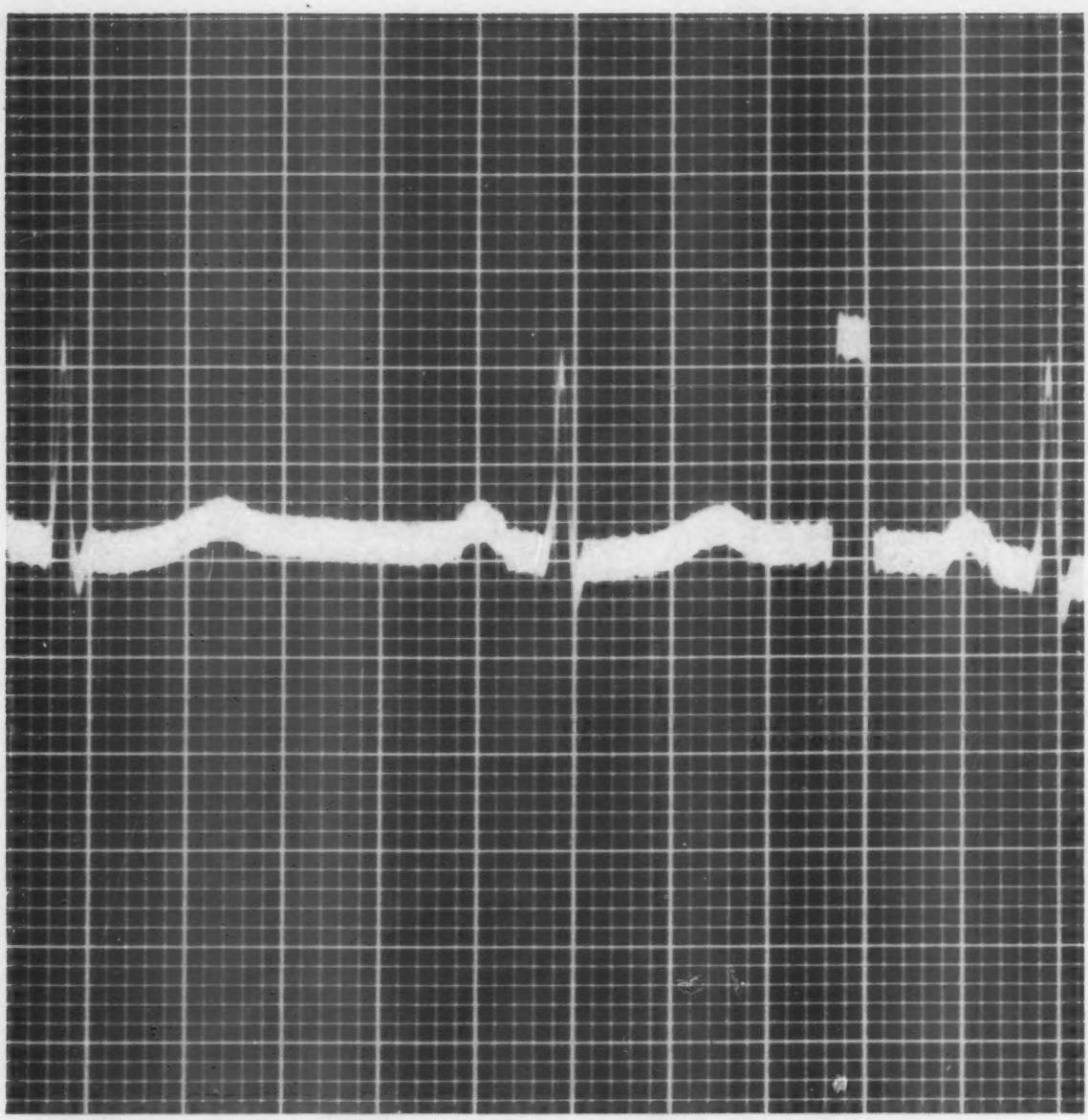

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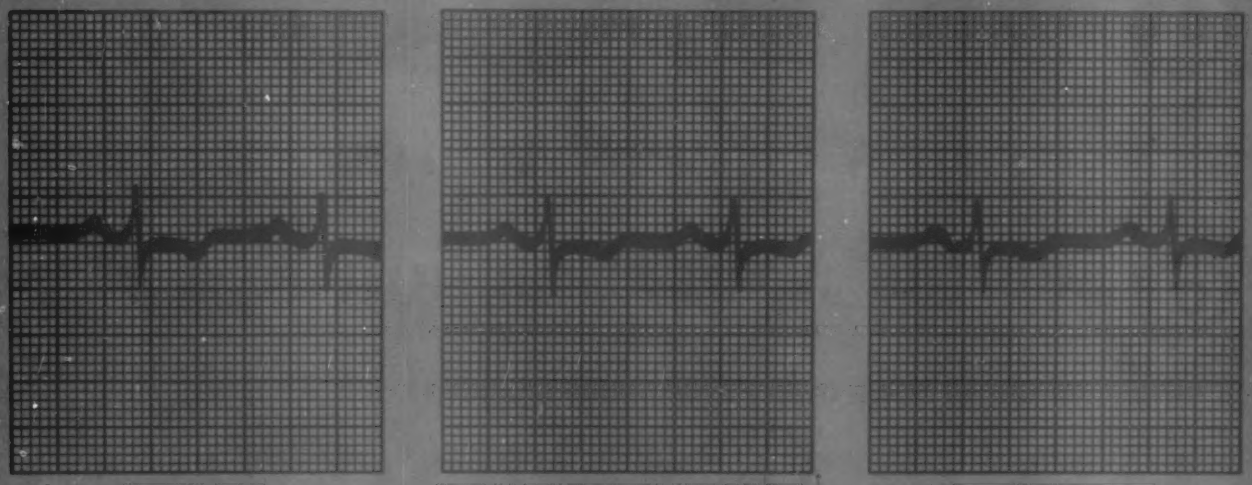

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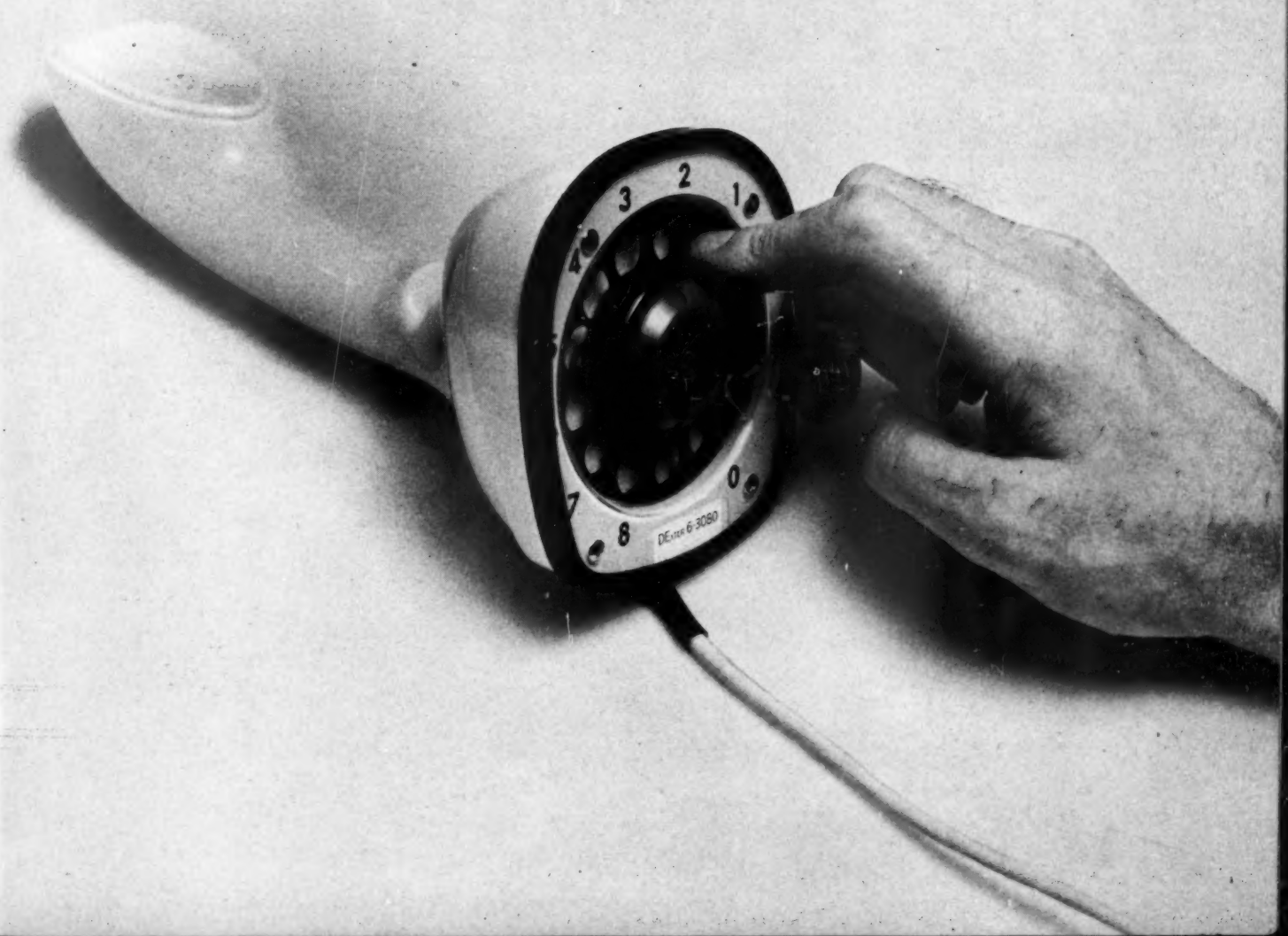

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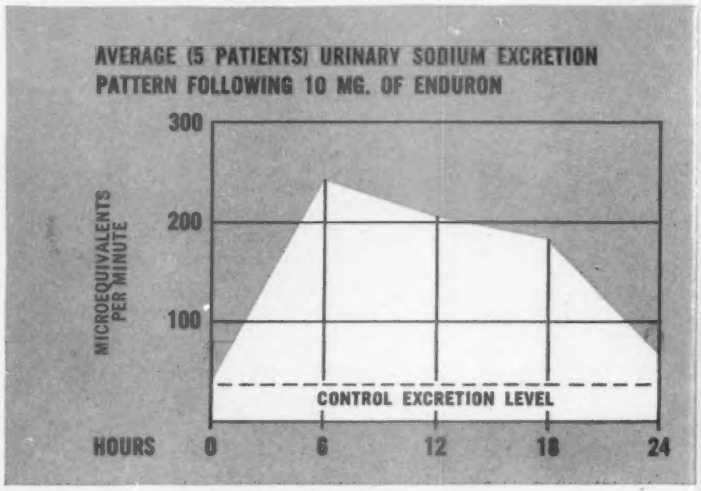

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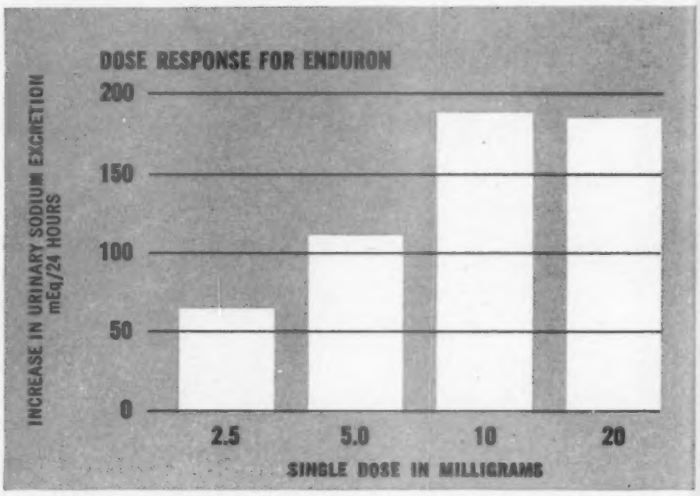

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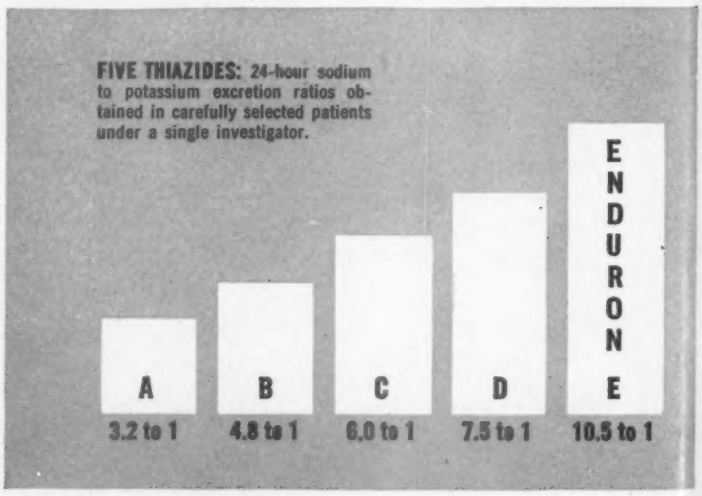

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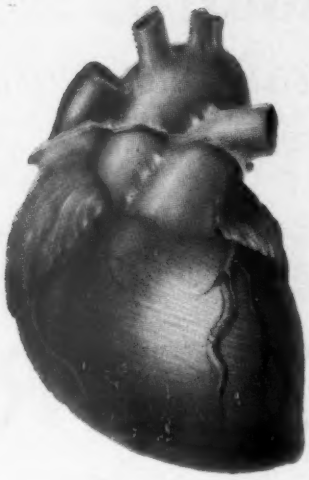

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REFERENCES

1. Ellis, L. B. *et al.:* Circulation *17*:945, May 1958. **2.** Friedlander, H. S.: Am. J. Cardiol. *1*:395, Mar. 1958. **3.** Riseman, J. E. F.: New England J. Med. *261*:1017, Nov. 12, 1959. **4.** Russek, H. I. *et al.:* Circulation *12*:169, Aug. 1955. **5.** Russek, H. I.: Am. J. Cardiol. *3*:547, April 1959. **6.** Tortora, A. R.: Delaware M. J. *30*:298, Oct. 1958. **7.** Waldman, S. and Pelner, L.: Am. Pract. & Digest Treat. *8*:1075, July 1957.

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The American Journal of Cardiology

VOLUME VII JANUARY 1961 NUMBER 1

Symposium on Pericarditis

Introduction

PERICARDITIS is not only an important disease but also one of widespread interest to general practitioners, internists, surgeons, pediatricians and roentgenologists.

Pericarditis must be differentiated from various diseases of the chest including spontaneous pneumothorax, pulmonary infarction, pleurisy, dissecting aortic aneurysm and, especially, myocardial infarction. It must be differentiated from acute upper abdominal surgical emergencies, particularly when the pain of pericarditis is abdominal and is accompanied by shock. Witherbee and Pearce[1] presented three patients with severe abdominal pain, two of whom also presented evidence of shock. Electrocardiographic changes were compatible with pericarditis in all three patients. An electrocardiogram and frequent auscultation before surgery are always indicated in abdominal conditions which appear to require surgery.

Pericarditis is frequently undiagnosed or misdiagnosed despite considerable dissemination of knowledge of this subject in recent years. Patients with pericarditis may be classified into two major groups: (1) those in whom pericarditis may be secondary to some general process, but symptoms relative to the pericardium dominate the clinical picture; and (2) those in whom pericarditis is part of a general clinical picture but predominant symptoms are elsewhere. As recently as 1958, Sodeman and Smith[2] noted that diagnostic accuracy was poor in the first group despite the obvious clinical picture of pericarditis. Of forty patients with a clinical picture of acute pericarditis, the diagnosis on admission was coronary occlusion in sixteen, pneumonia in eleven, rheumatic fever in two, pulmonary embolism in two, acute cholecystitis in one and acute pericarditis in only eight patients (a correct diagnosis of only 20 per cent of the patients). In the second group, with predominant symptoms elsewhere, diagnosis was even less accurate.

One should regularly examine patients for pericarditis in those conditions in which it frequently occurs such as rheumatic fever, myocardial infarction, uremia, disseminated lupus erythematosus, tuberculosis, pneumonia, pyogenic and viral infections and trauma to the chest. In fact, the finding of pericarditis in certain diseases, such as disseminated lupus erythematosus, may help establish the diagnosis of the major disease. A diagnosis of pericarditis, however, is not complete until the cause of the pericarditis is revealed although the specific cause cannot always be established. It is essential to determine the etiologic factors for prognosis and proper therapy, especially in view of the rapid expansion in the fields of antibiotic and chemotherapy. It is also important to know whether the process is acute, subacute or chronic constrictive. Surgery is eventually necessary in the constrictive process, and may be the treatment of choice in recurrent idiopathic pericarditis.[3] Surgical drainage, of course, should be considered in acute pyogenic infections.

CLINICAL FEATURES

Chest pain, the major symptom in all reports, is characterized by the fact that it often is exaggerated by body movement, respiration, coughing or swallowing. It may be severe, mild or even absent in up to 50 per cent of the patients, and depends primarily upon involvement of the pleural or diaphragmatic pericardium.

The pericardial friction rub is pathognomonic. It may be present continuously or intermittently for several days or longer or may be short-lived

or absent. It usually is heard best with the patient leaning forward and is accentuated by exerting pressure with the stethoscope.

Electrocardiographic changes depend upon the degree of myocardial involvement. Inflammatory involvement may range from practically pure myocarditis to pure pericarditis; therefore, electrocardiographic and clinical findings must vary from patient to patient and in the same patient from time to time. Repeated examinations are often necessary because of the variability of the clinical and laboratory pictures. Reports on large groups of patients with acute idiopathic pericarditis (AIP) indicate that from 40 to 80 per cent of the cases have suggestive to typical electrocardiograms.[4]

Serial roentgenograms of the chest may reveal changes in cardiac silhouette, even when the presence of pericardial fluid is not suspected.

Findings which may be considered pathognomonic of acute pericarditis are: (1) pericardial friction sounds, (2) typical serial electrocardiograms, (3) positive pericardial biopsy, (4) aspiration of inflammatory pericardial exudate and (5) demonstration of excessive pericardial fluid by x-ray films or catheterization (if hydropericardium, noninflammatory hemopericardium and chylopericardium can be ruled out).[4]

Etiologic Classification

The following is a rough etiologic classification of pericarditis:

A. Idiopathic or nonspecific
B. Infectious
   1. Bacterial
   2. Viral
   3. Fungal
C. The collagen-vascular group, including rheumatic fever, systemic lupus erythematosus, rheumatoid arthritis, and other diseases
D. Sensitivity states, including serum sickness, autoimmune reactions and various other allergic responses
E. Inflammations of contiguous structures, such as myocardial infarction, dissecting aneurysm, esophageal disease and pulmonary disease, especially pulmonary embolism and pneumonia
F. Neoplastic
G. Metabolic disorders (renal failure, etc.)
H. Traumatic, direct and indirect
I. Miscellaneous

In 240 cases of acute pericarditis, Sodeman and Smith[2] noted that 23 per cent were acute nonspecific, 17 per cent uremic, 16 per cent pyogenic, 11 per cent subsequent to myocardial infarction, 11 per cent rheumatic, 8 per cent neoplastic, 7 per cent tuberculous, 3 per cent associated with collagenic diseases, 3 per cent traumatic and 1 per cent unclassified.

Bacterial Infections: Since the advent of antibiotic and chemotherapy, viral infections have become more important and bacterial infections, in general, have become less important. The tubercle bacillus and the staphylococcus still are important organisms in the bacterial group. Pneumonia, which was the leading cause of pericarditis in 1901,[5] has been displaced by nonspecific pericarditis.

Idiopathic Group: The idiopathic or nonspecific group, no doubt, represents a group of disease processes, the major portion of which probably is viral, but in a large group, the process may represent hypersensitivity states or autoimmune processes. Other apparently idiopathic cases have been found to be caused by infectious mononucleosis, collagen diseases, particularly disseminated lupus erythematosus (DLE) and fungal inflammations, especially coccidioidomycosis, toxoplasmosis, histoplasmosis and moniliasis.

Allergic Pericarditis: Various clinical syndromes associated with pericarditis are now thought to be allergic reactions to exogenous and endogenous agents. These include serum reactions, collagen diseases, allergic vasculitides, the postmyocardial infarction syndrome, the postcardiotomy syndrome and the postcardiac trauma syndrome.

Viral Pericarditis: Many cases thought to be idiopathic are now being found to be caused by several specific viruses, especially influenza viruses (A and B)[6] and coxsackie viruses (A, B and different subtypes).[7] It is not surprising that respiratory viruses should be implicated frequently, because Rantz, Boisvert and Spink[8] stated that myocarditis complicated upper respiratory tract infections in 10.8 per cent of cases. With complement fixation tests and cold hemagglutinins, Silber[9] diagnosed heart disease due to viral infections in twenty-three patients, two of whom had pericarditis clinically. Both of the latter showed fourfold rise in influenza antibody titers. It is probable that any viral infection occasionally may produce acute pericarditis; pericarditis associated with mumps and chicken pox has been reported.

Infectious Mononucleosis: Although cardiac involvement in infectious mononucleosis has been reported in 1.5 to 41 per cent of the cases of infectious mononucleosis, pericarditis is not a common complication of this disease. However, more cases, no doubt, will be diagnosed when more physicians become aware that the disease is a cause of pericarditis. Webster[10] reported three cases of pericarditis complicating infectious mononucleosis. Shugoll,[11] not aware of Webster's cases, found eleven cases in the literature and added another.

Diagnosis of infectious mononucleosis *per se* is necessary before this etiologic diagnosis can be established, and this is difficult at times, especially when pericarditis is the initial manifestation. There is no specific test for infectious mononucleosis. With the combination of fever, lymphadenopathy, pharyngitis, splenomegaly, positive heterophil antibody agglutination and lymphocytosis with abnormal lymphocytes in the peripheral blood, one can be fairly certain of the diagnosis. Mason and Adams[12] considered the blood picture to be characteristic when 50 per cent or more of the total leukocytes were lymphocytes and when 15 per cent or more of the total leukocytes were atypical lymphocytes. They also considered an agglutination titer of 1:112 without absorption tests the most useful minimal heterophil reaction. Absorption tests are of value and increase the reliability of the heterophil test but are not infallible.

Fungal Infections: The fungal group also is becoming more important because of more specific methods of diagnosis and therapy and because some fungi, which previously were saprophytic, are becoming pathogenic. Fungal infections may be diagnosed by serologic and skin tests and recovery of the fungus itself. Fungi are weak antigens, therefore circulating antibodies are usually low. Various degrees of cross reaction with other fungi interfere with serologic interpretations; therefore, tests with antigens from related cross-reacting species should be made before a specific diagnosis is considered. Fortunately, these antigens generally do not react to antisera of bacteria, rickettsia or viruses; therefore, a positive serologic test indicates that a mycotic or fungal agent is probably the cause of the infection. The qualitative precipitation and agglutination tests usually are best for recently acquired infections, and the quantitative complement fixation test is the best for infections of long duration.[13] Specific skin tests for various fungal infections are extremely valuable, but are comparable to the tuberculin test; they only mean that the patient has been infected with that particular fungus. Evidence of fungal infection elsewhere should be searched for by cultures of blood, urine, bone marrow, lymph nodes, etc. and histologic studies of biopsy tissue.

Lupus Erythematosus: Herrmann et al.[14] found that in 130 cases of pericarditis there were four cases of disseminated lupus erythematosus (DLE), approximately 3 per cent. Griffith and Vural[15] noted seventeen cases of DLE in 19,242 autopsies, fourteen of which showed definite evidence of pericarditis. Disseminated lupus erythematosus pericarditis (DLEP) frequently has been diagnosed as acute idiopathic pericarditis (AIP), especially when pericarditis was the first overt sign of lupus. McQuiston and Moser[16] found that four (28.6 per cent) of their patients with DLEP on admission had had previous episodes of pericarditis which antedated other manifestations of DLE by periods of one and a half to twenty-two years. The two diseases may easily be confused because of many similarities; but when their differences are carefully considered, differentiation is less difficult. The incidence of recurrence, chest pain suggestive of pericarditis, fever, tachycardia, pericardial friction rub, pericardial effusion, pleural effusion, pulmonary infiltration and electrocardiographic changes consistent with pericarditis are somewhat similar in both. Antecedent infections of the upper respiratory tract are much more common in AIP, but pain in the joints, gastrointestinal symptoms, hypertension, anemia, congestive heart failure, skin rash, lymphadenopathy, hepatomegaly, splenomegaly, urinary abnormalities (albumin, casts, red blood cells) and false positive serologic tests for syphilis are all more likely to occur in DLEP. The findings in AIP are confined mainly to the chest, therefore, findings of other organ involvement speaks against this diagnosis. Leukocytosis predominates in AIP but a white count below 5000/cu. mm. is more common in DLEP. According to McQuiston and Moser,[16] serum globulins above 3.5 gm./100 ml. (mainly due to a rise in gamma globulin) occurred in 50 per cent of their patients with DLEP, but all the patients with AIP had serum globulins below this level.[16] None of their patients with AIP had a skin rash while 50 per cent of those with DLEP did, so this finding immediately suggested the

possibility of DLEP. Griffith and Vural[15] noted the typical butterfly rash in 61 per cent of their cases. Both diseases occur mainly in the younger age group. Women predominate 4 : 1 in DLEP, and men predominate by about the same ratio in AIP. Dubois[17] noted that 85 per cent of 400 patients with DLE were women and that the age of onset in most patients was from ten to forty years.

McQuiston and Moser[16] thought that the simple use of routine blood counts and urinalyses was the most significant means of separating these two disorders, but lupus erythematosus (LE) cells should be looked for in the blood, bone marrow or pericardial fluid of all patients with pericarditis. One should not rely on a single LE preparation because a subsequent test may be positive. False positive findings may occur, but negative tests occur in about 30 per cent of the patients with typical DLE. A positive LE test, of course, is practically diagnostic. When a rash is present, biopsies of the skin should be studied if necessary. Incidentally, systemic lupus should be considered for several years if a patient with apparent AIP happens to be a young female.

Staphylococcal Pericarditis: Although pyogenic pericarditis has decreased since the advent of chemotherapy and antibiotics because of the decrease in pneumococcal and streptococcal infections, staphylococcal pericarditis remains an important disease. Of twenty-seven cases of nontuberculous pericarditis in patients under twenty years of age seen from 1938 to 1956, fifteen were staphylococcal.[18] Men predominated and four were under one year of age. (During the same period there were only twelve cases in older persons.) Diagnosis was made clinically in twelve and at autopsy in three. It occurred as part of a general infection in all; pneumonia was the commonest associated lesion and osteomyelitis was the next. Positive blood cultures were obtained in fourteen. Correct diagnosis was suspected when positive staphylococcal blood cultures were obtained in the presence of cardiac enlargement or tamponade. Diagnosis was established by pericardiocentesis. Horan[18] recommended that when staphylococcal pericarditis is suspected, treatment with broad spectrum antibiotics such as chloramphenicol plus penicillin in large doses be started while waiting for blood cultures and sensitivity tests. Although Horan thought surgical drainage should be reserved for patients who, in spite of proper antibiotics, show recurrent tamponade or progression of pericarditis or develop resistant organisms, McGuire et al.[19] believed that purulent infections always require surgical drainage.

Rheumatic Pericarditis: Rheumatic and tuberculous pericarditis remain diagnostic problems, and rheumatic pericarditis is the most commonly considered problem in the diagnosis of idiopathic pericarditis. Murmurs, erythema marginatum, rheumatic nodules and a more protracted course aid in differentiating rheumatic cases, but occasionally it is impossible to differentiate them. Nay and Boyer[20] noted that pains in joints preceded the pericarditis in twenty-two of twenty-five patients with rheumatic pericarditis and that the P-R interval was prolonged in 30 per cent of those patients.

Tuberculous Pericarditis: Apparently tuberculosis is still thought to account for approximately 7 per cent of all cases of acute pericarditis. Herrmann et al.[14] found eleven cases of tuberculous pericarditis in 130 patients; however, Connolly and Burchell[21] noted only ten cases in 403 patients in their series. Patients with tuberculous pericarditis often have a prolonged course, sometimes stormy, with cardiac enlargement, distended neck veins and edema. T wave inversion tends to be persistent. The tubercule bacillus should be sought for by careful bacteriologic studies in all cases in which the pericarditis does not subside relatively soon, particularly if calcification of the pericardium or tuberculosis elsewhere is noted. It should be suspected in any patient with pericardial effusion but who appears well. In tuberculous pericarditis the effusion is characteristically slow in developing and often is massive in quantity. The tubercle bacillus should be sought in the pericardial fluid, but occasionally it may be necessary to perform pericardial biopsy which allows for drainage of the pericardial fluid as well as furnish tissue for microscopic examination and bacterial culture. Repeated negative tuberculin tests are of value. Therapy with para-aminosalicylic acid (PAS) and streptomycin permits earlier exploration and possibly pericardial resection than was considered safe a few years ago. Herrmann et al.[14] believe that surgery should be performed immediately after the acute process has subsided with medical treatment because of the frequency of subsequent constriction and invalidism.

Myocardial Infarction: Coronary occlusion, perhaps, is the most important diagnosis to

exclude in adults because of prognosis and therapy. Anticoagulants are indicated in coronary occlusion but contraindicated in pericarditis. Serial electrocardiograms with relatively widespread RS-T and T changes suggestive of pericarditis, absence of reciprocal RS-T changes in the standard limb leads, absence of Q waves, exaggeration of chest pain by respiration or body motions, and an early, often widespread pericardial friction rub help differentiate pericarditis from myocardial infarction. Infarction is less likely to be preceded by respiratory infection. Serum glutamic oxalacetic transaminase (SGO-T) levels usually rise by the second to third day and return to normal by the seventh day in patients with acute myocardial infarction. They are usually normal or only slightly elevated in pericarditis. The test is especially helpful if it is normal. Agress et al.[22] noted in dogs in which pericarditis was induced that the SGO-T levels varied with the extent of myocardial change.

Postmyocardial and Postcardiotomy Syndromes: Of recent interest has been the accumulation of information pertaining to the postmyocardial infarction syndrome of Dressler,[23,24] the post-commissurotomy[25] or postpericardiotomy syndrome[26] occurring after various cardiac traumatic states.[27] All are remarkably similar and suggest the possibility of autoimmune reactions.

Pericarditis associated with recent myocardial infarction usually is evanescent, usually appears between the second and fourth days of illness, does not recur, rarely is associated with pericardial effusion and is not associated with pleurisy or pneumonia. The friction rub in the postmyocardial infarction syndrome usually lasts three or four days to two or three weeks, usually occurs between the second and eleventh weeks of illness, is commonly associated with pericardial effusion, pleurisy and pneumonia and recurrences are a significant feature. The electrocardiogram in the postmyocardial infarction syndrome does not show evidence of extension of the infarction. Serial roentgenograms of the chest may reveal shrinkage of heart size. Anticoagulants are contraindicated in this syndrome, and adrenal steroids and the corticotrophic hormone are almost specific. Prognosis is good.[24]

Summary

1. Pericarditis is an important disease of interest in several branches of medicine. It frequently remains undiagnosed or misdiagnosed.

2. Diagnosis of pericarditis *per se* is not adequate. Diagnosis of the etiologic factor is essential for proper therapy and prognosis. It also is essential to know whether or not the condition is acute, subacute or chronic constrictive.

3. Acute idiopathic pericarditis still represents a group of etiologic factors, and should not be diagnosed until possible known factors have been eliminated.

4. Routine studies in pericarditis should include blood counts, urinalyses, blood cultures, chest x-ray films, skin tests for tuberculosis and fungal diseases, agglutination tests for the heterophil antibody and cytologic and bacteriologic examination of any aspirated fluid, biopsy or tissue. The tubercle bacillus, malignant cells and LE cells should be searched for diligently.

5. As virus laboratories become more prevalent, viral studies probably should become routine.

6. Pericardial biopsies probably should be used more freely.

7. Pericarditis should be searched for in any disease which may cause pericarditis, and extracardiac evidence of these diseases should be looked for when pericarditis is present.

8. If the patient is a young female, one should be alert for disseminated lupus erythematosus for several years unless the etiologic diagnosis has been established.

9. Treatment depends upon the etiologic diagnosis and the particular stage or type of pericardial syndrome present in each case.

From the incomplete but relatively extensive outline of etiologic factors presented in this discussion and the obvious possibility of pericarditis being caused by numerous agents, many previously reported but not presented here, it seemed impractical to publish articles on each individual etiologic factor. Starting with such a premise, this Symposium is presented in the interests of the various disciplines of medicine, not only by bringing new information from various recognized authorities but also by reviewing many features which may be well known to many of our readers.

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Pericarditis: A Ten Year Survey*

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PATIENTS' RECORDS indexed in the files of the Mayo Clinic by the diagnosis pericarditis (or suspected pericarditis) during the ten years 1950 to 1959 inclusive were obtained and the clinical and laboratory data on such patients were reviewed. The main objectives of the study were evaluation of the incidence and natural history of acute nonspecific pericarditis, and comparison of the incidence of this with other forms of pericarditis. It was anticipated that in some instances the modifying adjective "nonspecific" might be discarded, or that at least the etiologic factors might be more clearly defined.

In the original report from this clinic[1] relating to a form of acute pericarditis, believed nonbacterial and without established cause, it was stated that a viral cause was believed likely to have been present. The history and evidence of an associated pleuritis or pneumonitis or both in many cases supported a viral cause, and in others the reaction suggested a hyperergic pericardial response to a nonspecific stimulus. Since that time the identification of viral infection in many cases has been established by numerous reports in the literature, a Coxsackie virus being most commonly reported.[2–8] In the present series the likelihood of a viral cause in many was preeminent, but with the absence of proof the majority of our cases must remain in the nonspecific or idiopathic category. The importance of possibly associated pneumonitis and myocarditis has been repeatedly emphasized by various reports and we would concur in such a view.

Recently, the postcardiotomy syndrome[9] and the postmyocardial infarction syndrome[10] have been established as clinical entities, although the etiologic mechanisms need further clarification. Evidence is accumulating to support the inclusion of these syndromes in the group of autoimmune diseases, with the laboratory evidence that, in such cases, high titers of specific heart autoantibodies may be found.[11]

The cardiologic group at the Mayo Clinic has long had an interest in pericarditis associated with, and following, myocardial infarction, but a delayed pericarditis was not recognized as a complication in proper perspective until after the papers of Dressler were published.[10] In our experience the postmyocardial infarction syndrome of pericarditis is rare, but a constant challenge to the diagnosis of acute nonspecific pericarditis is the pertinent question as to whether a small unrecognized "silent" myocardial infarction might have preceded the more dramatic illness related to the pericarditis. We have reviewed the records of those patients constituting the background for Barnes' report on myocardial infarction complicated by pericarditis,[12] and in one case the possibility of postmyocardial infarction pericarditis was suggested by the history; in each of the others it was clear that the pericarditis and the infarction were coexistent within the same week.

An important clinical problem at this time is the relative frequency with which nonspecific pericarditis is suspected and the difficulty of establishing the diagnosis in the patient not seen during the course of his acute illness. If careful auscultation is not carried out and if frequent electrocardiograms and adequate roentgenograms are not obtained during the acute episode, the opportunity of making the diagnosis may be lost. The medical literature is replete concerning these problems, which are not new but have taxed the abilities of clinicians for decades, and the frequency of, and approaches to, the problem in previous years have been reviewed by Christian[13] and others.[14–20]

Concerning the first series of fourteen cases of acute pericarditis mimicking acute myocardial infarction, reported by Barnes and one of us,[1] there has been no new evidence that would necessitate any change in the original diagnosis

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TABLE I
Distribution of Patients by Type of Pericarditis and by Sex

Group	Male	Female	Total	
I. (A). Acute nonspecific pericarditis without effusion				
1. By history alone	32	29	61	175
2. By history and observation immediately subsequent to episode or relapse	53	18	71	
3. By observation during entire episode	35	8	43	
I. (B). Acute nonspecific pericarditis with effusion (pericardial, pleural, or both)				
1. By history and observation immediately subsequent to episode or relapse	18	9	27	94
2. By observation during entire episode	37	30	67	
II. Pericardial effusion with tuberculosis	4	—	4	
III. Chronic pericarditis				
1. Chronic constrictive pericarditis	53	26	79	92
2. Calcific pericarditis without constriction	8	5	13	
IV. Chronic pericardial effusion				
1. Idiopathic	0	9	9	13
2. Associated with congenital heart disease	0	3	3	
3. Cholesterol pericarditis	0	1	1	
V. Postmyocardial infarction syndrome	7	0	7	
VI. Pericarditis associated with radiation therapy	4	4	8	
VII. Pericarditis associated with rheumatoid arthritis	6	4	10	
Total			403	

and general conclusions drawn regarding the clinical picture, including the tendency toward relapse and for eventual complete recovery to occur. Our experiences in recent years, however, have indicated clearly that occasional patients who have typical acute nonspecific pericarditis clinically may develop, within a few months, a constrictive pericardial syndrome, as others[21,22] also have reported. In addition, the tendency to frequent relapses in certain patients has led to corticosteroid therapy, and a few patients have been seen with severe hypercorticoadrenalism and corticosteroid dependency, creating a new troublesome syndrome.

The introduction of surgical resection of the pericardium as a method to prevent relapses is an acknowledged advance if restricted to highly selected cases.[23,24] We have discussed such therapy in a number of cases, and offered it to three patients in the past two years without its being accepted.

Pericardial biopsy has been done more frequently by us in recent years; although in the initial cases selected the condition was often diagnosed (particularly neoplastic or tuberculous pericarditis), recently the utilization of biopsy more generally and in larger series has only rarely afforded diagnostic help. Such studies, however, have been limited to the routine type of histologic examination and to routine culture for the usual bacteria and fungi. Whether myocardium might not also be obtained in selected cases for study is a question that may well be answered eventually in the affirmative.

From this report are omitted cases of pericarditis related to uremia, metastatic carcinoma, rheumatic fever, the florid stage of lupus erythematosus, and the late stages of debilitating diseases. It must be recognized that on rare occasions metastatic carcinoma may make its debut by what would appear to be an innocent type of pericarditis. With these cases omitted, our total series of patients with the diagnosis of pericarditis may be categorized and enumerated as in Table I.

ACUTE NONSPECIFIC PERICARDITIS

The problem of diagnosis of acute nonspecific pericarditis frequently arose in the group of

patients who were not seen during or soon after the acute episode and in whom the diagnosis was made by history alone, often with review of the pertinent electrocardiograms and a report of the relevant clinical and laboratory data. It seems likely that many patients with bona fide acute nonspecific pericarditis were omitted from this group because of inadequate evidence. The diagnosis appeared to be well founded in all of the patients seen in or immediately subsequent to an acute episode.

The patients with acute pericarditis were arbitrarily divided into two categories: (A) those without evidence of pericardial or pleural effusion and (B) those with evidence of pericardial or pleural effusion or both.

Without Effusion: The study indicated that, in general, those patients in whom evidence of effusion did not develop appeared to have a more benign type of disease, and it was thought also that patients with effusion might prove subsequently, on the basis of long term follow-up, to have more difficulty as a result of their disease. In several patients the pericardial effusion persisted for long periods, but since it appeared to follow an episode of acute nonspecific pericarditis these patients have been retained in the acute pericarditis group. The comparatively large number in this group (175 cases) may be related to the likelihood that patients with more prolonged and troublesome disease processes might have had a greater tendency to seek medical help than did patients whose disease ran a brief course. The criteria for diagnosis of pericardial and pleural effusion rested largely on roentgenographic evidence, and this group includes some patients with minimal effusion.

In the category of patients without effusion, males predominated over females by a ratio greater than 2:1. A history of preceding infection of the respiratory tract was obtained in only thirty-nine of the 175 patients, but the number of patients giving such a history was greatest among those observed here during the entire episode—eighteen of the forty-three patients. A history of recurrent episodes of acute pericarditis was obtained in twenty-six of the 175 patients, and again the frequency of such a history was greatest among the patients observed here during the entire episode. We have seen no evidence of any relation to a geographic or occupational factor.

In four of the patients the episode of acute pericarditis occurred after a surgical procedure —abdominal in two cases and minor in two.

With Effusion: As noted previously, these ninety-four patients were separated from the main group because of the presence of pericardial or pleural effusion, or both, and it was thought probable that in these there was evidence of a more advanced disease process. Parenthetically, in certain instances the possibility of dilatation of the heart itself due to an associated myocarditis creates a secondary diagnostic problem.

Of the ninety-four patients, thirty-six gave a history of preceding infection of the respiratory tract and thirty-six had recurrent episodes of pericarditis.

Aspirations of pericardial or pleural fluid or both were carried out for therapeutic or diagnostic reasons in twenty-seven patients; fifteen had aspiration of pericardial fluid, and fifteen aspiration of pleural fluid. No detailed analysis of the findings on examination of a large number of these specimens of pericardial fluids has yet been made, such as that made on pleural fluids.[25]

In eighteen patients, partial pericardiectomy was performed. In none of these was a definitive diagnosis established on the basis of routine study and culture of pericardial fluid or tissue.

In three patients there was evidence strongly suggesting that histoplasmosis was the etiologic factor; two of these patients had caseous granulomatous lesions of the mediastinum which gave negative results on culture, while all three patients had strongly positive skin reactions for histoplasmosis. Billings and Couch[26] have reported studies relating histoplasmosis to pericarditis.

In one patient there was evidence suggesting coccidioides as the causal agent; the patient had recently stayed in the San Joaquin Valley of California, had x-ray evidence of pulmonary infiltration, and gave a positive reaction with the coccidioidin skin test. This type of problem has been reported by Larson and Scherb.[27] One patient, aged one year, was found at necropsy to have a sterile pyogenic pericardial effusion, partly organized.[28] In one patient, Micrococcus pyogenes was cultured from his pericardial effusion. One patient had pulmonary aspergillosis with purulent pericardial effusion. In one patient the diagnosis of sarcoidosis was made one year later. Two patients with pericardial effusion also had fibroma of the ovary.

This group of ninety-four patients does not include four patients with pericardial effusion from whom Mycobacterium tuberculosis was isolated. The four patients in whom chronic constrictive pericarditis developed subsequent to typical acute nonspecific pericarditis have been included in the category of constrictive pericarditis.

Chronic Pericarditis

Chronic Constrictive Pericarditis: This diagnosis was made in seventy-nine patients during the ten year period. The ages of the patients ranged from eight to seventy years. Of these patients, sixty-five had pericardiectomy. The remaining fourteen patients either were advised to have operation and they refused, or they were advised against operation because of extreme debility or the relatively mild nature of their symptoms. A review of many of these operative cases has been published previously.[29] There were several interesting features in this group from the point of view of the present study: In four patients chronic constrictive pericarditis developed within a relatively short time of the occurrence of typical acute nonspecific pericarditis, the diagnosis of cardiac constriction being made $2^1/_2$ months, four months and four years, respectively, after apparently typical acute nonspecific pericarditis in the first three of these patients. The fourth patient had the initial episode of acute pericarditis in 1951, with recurrences in 1952 and 1954. Each of these episodes was observed at the Mayo Clinic. The diagnosis of chronic constrictive pericarditis was made, and pericardiectomy was performed successfully in August 1955.

In one additional patient with mitral stenosis who had acute nonspecific pericarditis in July 1953, an "adhesive pericarditis obliterating the pericardial sac" was found at the time of mitral commissurotomy in November 1954. However, this adhesive pericarditis had not caused cardiac constriction. (This patient has been included in the acute pericarditis group.)

In only six of the surgically treated patients was Myco. tuberculosis isolated from cultures of the pericardium or adjacent lymph nodes.

One patient with calcific pericarditis with constriction had findings suggesting the possibility of histoplasmosis as the etiologic factor—disseminated calcific nodules in both lung fields and a strongly positive histoplasmin skin reaction. One patient had diffuse pulmonary fibrosis, and another had a diffuse granulomatous disease of the lung, both of undetermined cause, in association with constrictive pericarditis. Three patients had constrictive pericarditis in association with atrial septal defect.[30] Three patients had constrictive pericarditis in association with chronic rheumatic mitral valve disease. Three patients with chronic constrictive pericarditis had a typical nephrotic syndrome.[31] In one of these patients the evidence of the nephrotic syndrome had disappeared eight weeks after operation.

Calcific Pericarditis without Constriction: In thirteen patients there was x-ray evidence of pericardial calcification. In one of these there was a previous history of severe trauma to the thorax with probable hemopericardium, and in three there was a history suggestive of previous pericarditis.

Chronic Pericardial Effusion

Nine patients, all female, in this group had chronic idiopathic pericardial effusion. None showed evidence of cardiac tamponade. The findings in six of these patients have been published previously.[32] In three other female patients, pericardial effusion was associated with congenital heart disease;[30] there was no history suggesting acute nonspecific pericarditis in these patients. The diagnosis of cholesterol pericarditis was made in only one patient in this ten year period, the clinical picture being that of congestive heart failure of long duration.

Postmyocardial Infarction Pericarditis

This syndrome was considered the probable diagnosis in seven patients, all males. All had previous historical or electrocardiographic evidence, or both, of coronary artery disease, and all had evidence of subsequent acute pericarditis. However, the diagnosis was considered to be fairly certain in only three of these patients, one of whom had recurrence of pericarditis with effusion, or acute pleurisy, on four occasions during the year following his acute infarction.

The diagnosis of postinfarction pericarditis was considered strongly in several other patients in the group with acute nonspecific pericarditis, but was rejected because of lack of evidence.

Pericarditis Associated with Radiation Therapy

This occurred in eight patients. In all

cases the pericarditis followed application of roentgen rays to the mediastinal or left thoracic region. In two patients the clinical picture was that of chronic constrictive pericarditis which appeared years after massive doses of x-rays to the region of the left breast and to the mediastinum, in cases of carcinoma of the left breast and testicular tumor, respectively.[33] In the remaining six patients, conclusive evidence of acute pericarditis appeared during the course of therapeutic radiation of the thoracic region. In one patient acute pericarditis developed during each of two courses of x-ray therapy to the thoracic region, the courses being separated by an interval of two months.

Pericarditis Associated with Rheumatoid Arthritis

In ten patients the picture of acute pericarditis developed during the course of rheumatoid arthritis, and two additional patients, not included in this group, acquired rheumatoid arthritis some years after what was apparently an episode of acute nonspecific pericarditis.

Of the ten patients with rheumatoid arthritis, seven were receiving adrenal steroids at the time of occurrence of the pericarditis and one of these patients presented the picture of hypercortisonism from overdosage of adrenal steroids. Exploration of the thorax was performed on two patients, each of whom had evidence of pleural disease; in one an edematous-appearing fibrin clot obliterated the pleural and pericardial space, and in the other a grayish turbid fluid was present in the pleural space, and the pericardium was adherent.

It is pertinent to mention that, in emphasizing that rheumatoid arthritis is a generalized disease, rheumatoid nodules in the pericardium have been described by Bauer and Clark.[34]

Comments

In patients with a subacute illness characterized mainly by pericarditis, three outstanding etiologic factors that have been carefully considered in our practice are tuberculosis, lupus erythematosus and neoplastic disease, but even these three causes combined add up to a small minority of the total causes.

In the patients with pericarditis as the only finding but with the strong diagnostic suspicion of systemic lupus erythematosus present, clot tests for lupus erythematosus gave negative results; this test would appear not to pay dividends as an etiologic screening test. In one case the results of this test became positive after two months of progressive illness, but at the time of the initial pericarditis the result was negative. In one case pericarditis occurred in a hypertensive patient undergoing treatment with hydralazine, and in this patient the lupus erythematosus clot test gave a positive result.

The tuberculin skin test has been given to the majority of patients but has only rarely been of real diagnostic help.

Steroid Therapy in Acute Nonspecific Pericarditis: The treatment of acute nonspecific pericarditis is usually that of the initial transient acute symptoms. However, the problem of treatment becomes more complicated when there are recurrent episodes of pericarditis which may incapacitate a patient for long periods. Adrenal steroid therapy has been advised and found very useful for alleviation of the acute symptoms in some patients with nonspecific pericarditis. Unfortunately, new problems may arise as a result of this treatment. We have seen twenty-seven patients who have been treated with adrenal steroids for acute nonspecific pericarditis. In eighteen the duration of treatment was brief and the dosage moderate. However, in nine there was dependence on adrenal steroids to the extent that a recrudescence of symptoms of acute pericarditis occurred with cessation of such treatment, or in some cases it was necessary to institute a prolonged program of steroid therapy with very gradual reduction of dosage. Three of these nine patients had severe hypercorticoadrenalism following administration of steroids for a period of three years.

Illustrative Case: A physician's wife, aged thirty-eight, was first seen at the Mayo Clinic in May 1957 during the fifth episode of a stereotyped acute illness characterized by fever, severe malaise, tachypnea and an anterior pleuritic type of pain. The first episode had occurred in September 1956, and this and the second one had subsided with treatment consisting of rest and use of an aspirin compound. Steroid treatment was given first with the third episode in December. It was given also for the fourth episode, in February; and when a maintenance dose of prednisone was gradually reduced from 15 to 7.5 mg. daily, the fifth episode occurred which promptly subsided on resumption of the daily dose of 15 mg. (5 mg. three times a day).

The patient was at home for six months, returning to the clinic in October, when she reported that she had had four additional episodes of fever, pain and weakness and that she was being maintained on a schedule of ACTH, 20 units daily, and prednisolone, 20 mg. daily. With most attacks she had had a peri-

cardial rub, and the electrocardiogram had been indicative of pericarditis.

On the second admission there were signs of a moderate hypercorticism, with some rounding of the face, acne and hirsutism. The change in appearance was particularly devastating to the patient's morale, and on one occasion she had suffered an acute psychotic episode. She returned in order that the question of pericardiectomy or further manipulation of corticosteroid dosage, or both, might be considered. Even with very slow reduction in dose she had recurrence of fever, evidence of pericarditis and increase in sedimentation rate whenever the dose was dropped to the neighborhood of 16 mg. of prednisolone daily. After five months of observation in the hospital she was dismissed with instructions to continue taking 17.5 mg. daily. At no time did she have anemia, leukopenia or positive results with the lupus erythematosus clot test.

Repeated reports from the patient indicate that she has continued taking a maintenance dose of 17.5 mg. of prednisolone daily and has had moderate hypercorticism. In April 1959 total hysterectomy was performed for menorrhagia and a large fibroid, without complication. In the last report in January 1960, she and her husband were said to be semisatisfied with her state and dreaded thought of any further attempt to reduce the steroid treatment or of surgical excision of the pericardium.

Surgical resection of the pericardium deserves serious consideration in the presence of recurrent pericarditis to prevent further recurrences, and also to prevent the complications resulting from the use of adrenal steroids in large doses over a prolonged period.

Steroid Therapy in Postcardiotomy Pericarditis: Our experience with adrenal steroid treatment of postcardiotomy pericarditis is similar to that in acute nonspecific pericarditis. Of forty patients in whom the diagnosis of the postcardiotomy syndrome was made, thirteen were treated with adrenal steroids. Eleven received these drugs in moderate dosage over a short period, but the other two became steroid-dependent. One of the latter two patients also had evidence of hypercorticoadrenalism; the other has taken adrenal steroids in relatively small dosage for four years following mitral commissurotomy but each attempt to stop administration of steroids has been followed by a recurrence of acute symptoms. Resection of the pericardium for such recurrent disease becomes a more serious procedure in the case of the postcardiotomy syndrome because of the presence of underlying valvular heart disease. (Data on the forty patients thought to have postcardiotomy pericarditis have not been included in Table 1 mainly because not all these patients were examined here subsequent to the development of symptoms.)

Myocarditis and Pericarditis: Myocarditis occurs in a small but definite proportion of patients in association with acute nonspecific pericarditis, and it appears that the etiologic agent must be viral in most of these patients.[8,35] We have seen four patients whose illness began with apparently typical acute nonspecific pericarditis and who subsequently developed definite evidence of myocardiopathy. In two additional patients whose clinical state seemed to be primarily that of myocardial failure there was evidence of both pericarditis and myocarditis at necropsy. Myocardial biopsy has been considered in some of these patients, but has not as yet been offered to a patient. (This group of patients seems to be different from our larger group of patients with idiopathic cardiac enlargement and failure, in some of whom pericardial exploration and biopsy have been carried out.) Steroid therapy might be expected to have a beneficial effect, theoretically at least, in this group of patients thought to have viral pericarditis and myocarditis, but we have no evidence that such an effect would actually be obtained.

Purulent Pericarditis: In our series of patients the number with purulent pericardial effusion is strikingly small, and is undoubtedly related to the widespread early use of antibiotics for febrile illnesses. Only two patients with purulent pericardial effusion are included in Table 1. An additional patient, not included, had a septic acute myocardial infarction with rupture of the abscess into the pericardium, causing a purulent effusion. Similarly, the incidence of tuberculous pericarditis has declined greatly, a total of only ten established cases being encountered in this series of 403 patients.

Hemopericardium: Traumatic pericarditis has been uncommon in our practice, only one patient with this diagnosis having been seen in ten years. However, hemopericardium due to cardiac rupture following acute myocardial infarction, trauma and rupture of dissecting hematoma of the aorta into the pericardium has been seen frequently, but is not included in this series of patients with pericarditis. In the whole series of 403 patients, there were no deaths due to pericardial hemorrhage following acute nonspecific pericarditis. The possibility of such a complication is well recognized and would appear facilitated by anticoagulants

were these given with the mistaken diagnosis of myocardial infarction.

Pericardial effusion in association with uremia and metastatic carcinoma has been seen very frequently, but these patients also have not been included in this series. Some of the patients not included have been of interest, however: in three, pericardial effusion was associated with hemangiopericytoma, and in two it was associated with thymoma.

Summary

Acute nonspecific pericarditis is a relatively common diagnosis, and probably represents a group of disease processes. The etiologic agent in many patients is a virus, and in a large group of patients the process is related to a hypersensitivity state or an autoimmune process.

Acute nonspecific pericarditis is not always a benign disease, although in the majority of patients it runs a benign course. Among the complications that may result are pericardial effusion with tamponade, pericardial hemorrhage, acute relapses, the subsequent appearance of chronic constrictive pericarditis, and the occurrence of associated myocarditis.

Adrenal steroid therapy may help dramatically in some patients, but steroid dependence and occasional hypercorticoadrenalism are disturbing complications of this treatment.

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Auscultatory Findings in Diseases of the Pericardium*

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Auscultation of the heart is of great help in indicating disease involving the pericardium and frequently provides the first clue to the correct diagnosis.

Pericardial Friction Rub

Acute pericarditis from various causes can be diagnosed readily by the characteristic friction rub.[1,2] As a rule, this friction rub is of a scratchy or grating quality, having components with higher frequencies than most organic heart murmurs and often sounding more superficial or closer to the ear. The typical pericardial friction rub has two or three components (Figs. 1 and 2). *The first component* (provided there is normal sinus rhythm) is related to atrial systole and results in a friction component in presystole. This is usually distinct and ends before the first heart sound. *The second component* is related to ventricular systole and produces a systolic friction rub. It is often the loudest of the components, although the atrial portion is sometimes of greater intensity. *The third component* of the friction rub generally occurs in early to middle phase of ventricular diastole, apparently coinciding with the time of rapid filling.

The fully developed friction rub having these three components is the most characteristic, not specific to any primary cause. This particular sequence of the various components seems responsible for the auscultatory characteristics of a friction rub, and is simulated by rubbing together rough surfaces such as wood and sandpaper with several short interrupted strokes, or the creaking of leather. Usually it is not a continuous quality, particularly because of the short gap between the atrial component in presystole and the ventricular systolic component.

Sometimes only two components are audible. If the rhythm is regular, the friction components are related to atrial systole and ventricular systole. If the rhythm is irregular with atrial fibrillation, thereby having no atrial component, a rub having two parts is produced in ventricular systole and diastole (Fig. 3). Occasionally, with atrial fibrillation a systolic component only is evident. One friction component in systole may be an early indication of pericarditis, with the diastolic components appearing subsequently. One should hesitate in making the diagnosis of acute pericarditis by hearing only this one component. However, the persistence of a systolic component alone in the presence of normal sinus rhythm generally eliminates the possibility of a friction rub. A more scratchy systolic murmur over the pulmonary area or left sternal border is at times erroneously diagnosed as a pericardial friction rub. In one patient, observed over a period of eight years, a diagnosis of pericarditis had been initially suspected on several hospital admissions because of such a murmur.

The pericardial friction rub is usually best heard along the lower left sternal border, xiphoid or lower sternal areas, with the patient sitting upright, leaning forward, holding his breath in deep expiration. Occasionally, it is heard better by having the patient lie on his abdomen propped up on his elbows, breath held in deep expiration. Occasionally, there is a variation of the friction rub consistent with respiration, generally increasing with respiration as shown in Figure 4. It is, therefore, advantageous to listen during normal respiration as well as during deep-held expiration. The friction rub is usually characteristic and should not be mistaken for an

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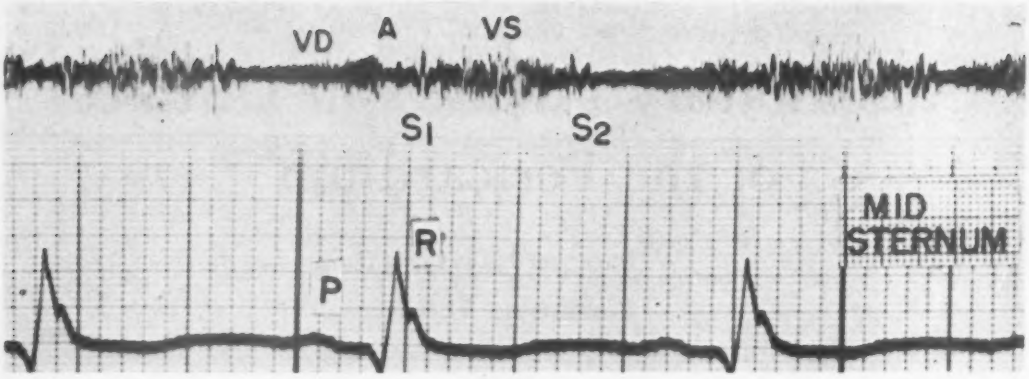

FIG. 1. Friction rub in a seventeen year old boy with uremic pericarditis. Note the three components: Atrial (A), ventricular systole (VS) and ventricular diastole (VD). First sound (S_1), and second sound (S_2).

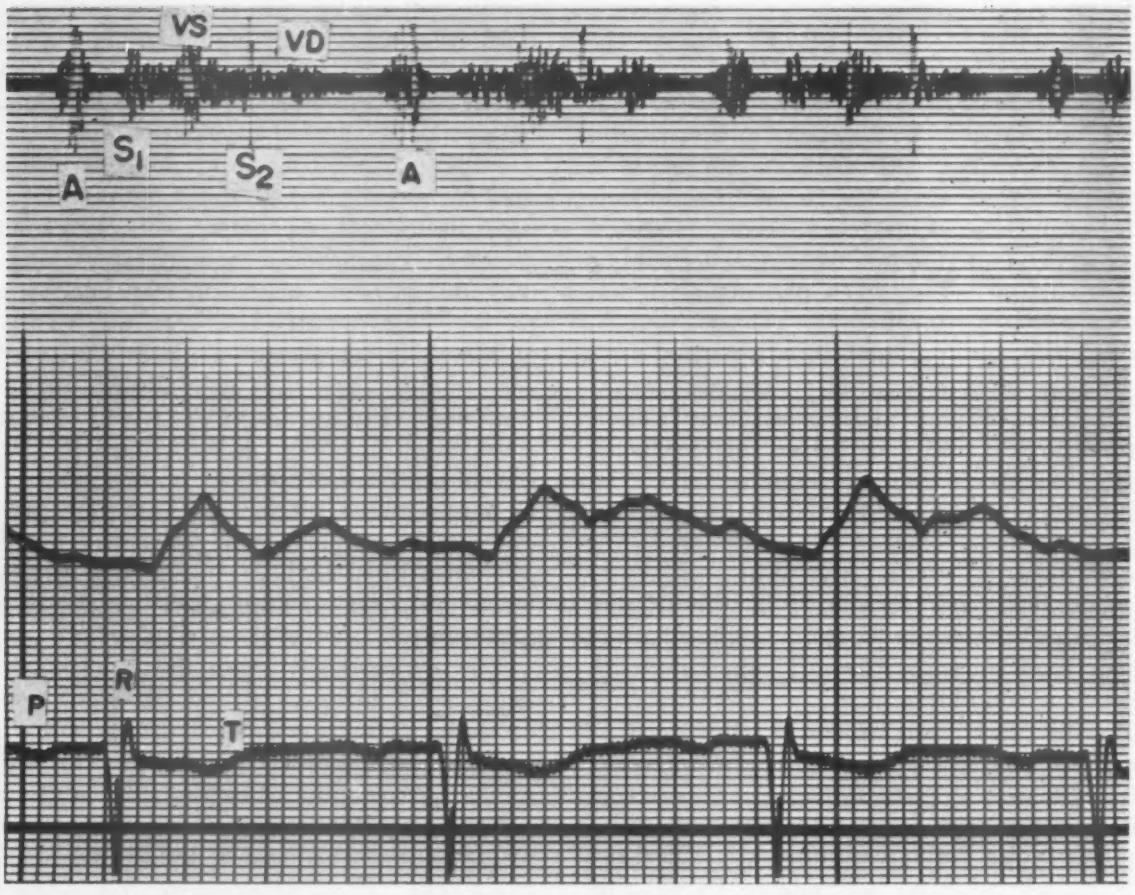

FIG. 2. Friction rub in a twenty-two year old man with acute benign pericarditis. Three components of pericardial friction rub are present. Atrial (A) and ventricular systole (VS) were loud. Ventricular diastolic component (VD) was fainter. First sound (S_1); second sound (S_2).

organic heart murmur. On occasion, however, such confusion may exist (Fig. 4). This figure was obtained from a patient with chronic glomerulonephritis and uremic pericarditis. He was known to have uremia and a loud pericardial friction rub with a prominent high-pitched blowing diastolic component. A wide pulse pressure was also present and some observers suspected the presence of aortic insufficiency superimposed on pericarditis. Postmortem examination revealed only acute fibrinous pericarditis and all heart valves were normal.

A pericardial friction rub during the course

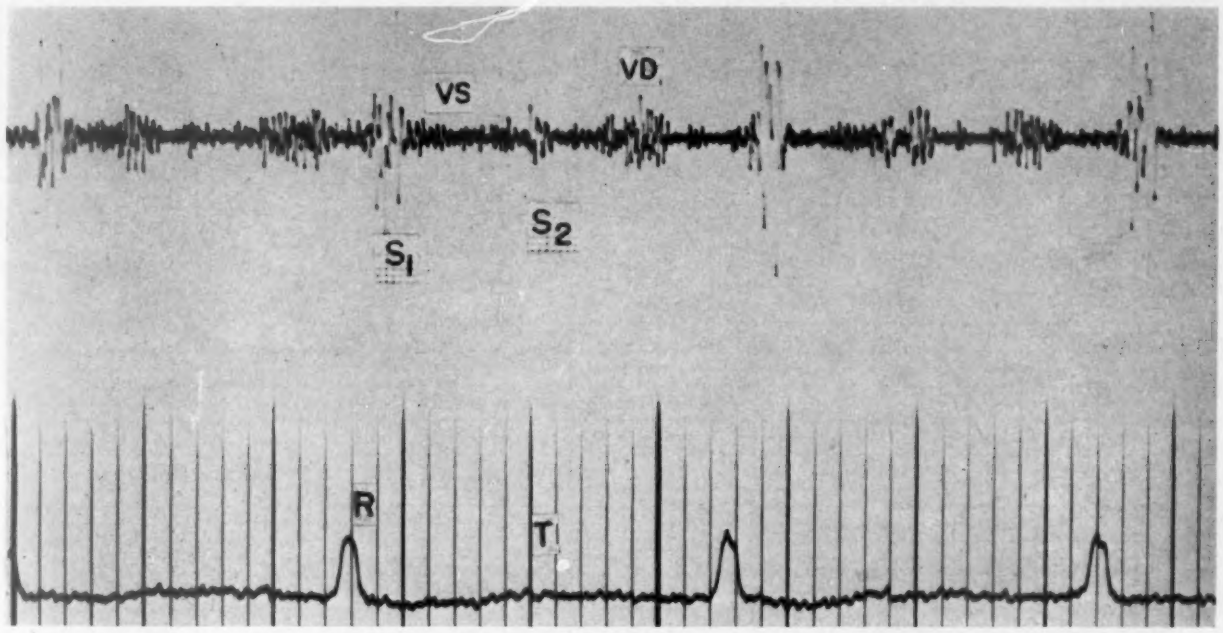

FIG. 3. Pericardial friction rub in a woman occurring after surgery for mitral insufficiency. Atrial fibrillation and two major friction components are present: Ventricular systole (VS) and diastole (VD). No atrial component.

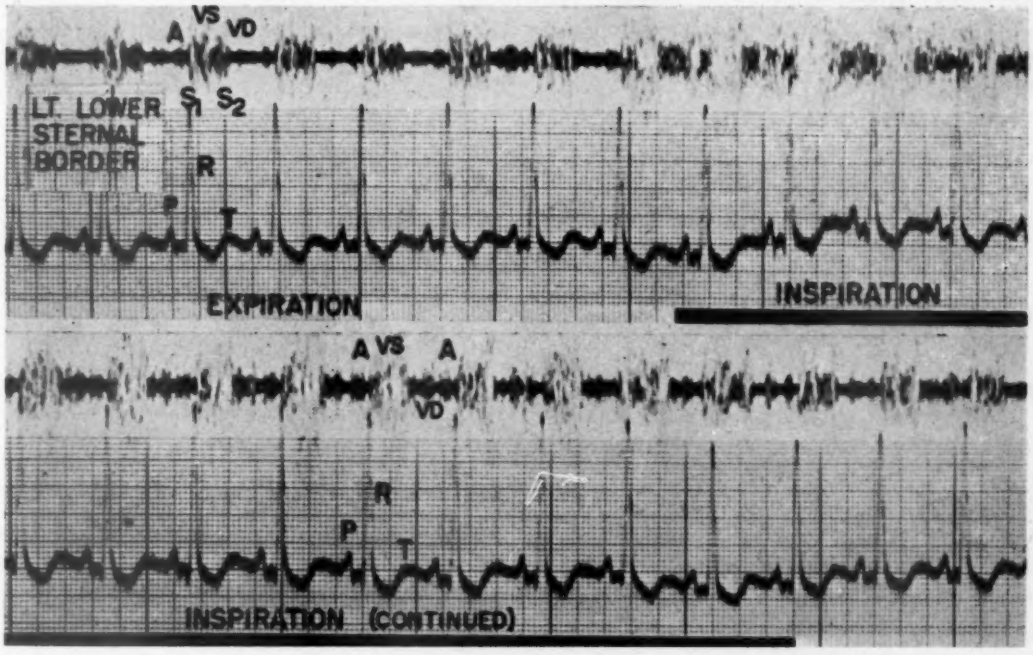

FIG. 4. Friction rub in a forty-six year old man with uremic pericarditis. Three components of friction rub are present: Atrial (A), ventricular systole (VS) and ventricular diastole (VD). Significant increase in intensity of friction rub occurs with inspiration.

of acute myocardial infarction is usually transient, lasting hours to several days as compared with the friction rub of acute benign pericarditis, which is likely to persist for a number of days or occasionally several weeks. A new friction rub during the course of an acute myocardial infarction when the patient is receiving anticoagulants should always suggest the possibility of hemorrhagic pericarditis. A combination of significant elevation of temperature and a loud friction rub is frequent. A pericardial friction rub is sometimes heard after cardiac surgery when the pericardium has been opened. For example, a pericardial friction

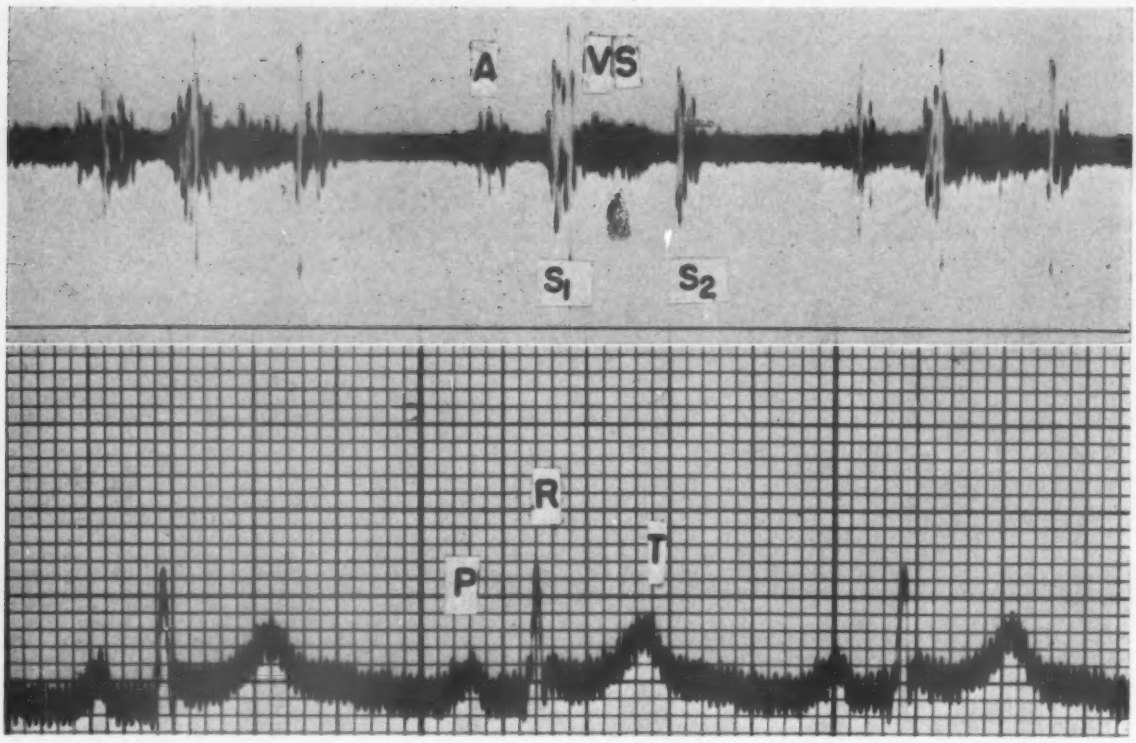

FIG. 5. Postoperative friction rub in a twenty-eight year old woman one day after surgery for tight mitral stenosis. Transient friction rub lasting several days having atrial (A) and ventricular systolic (VS) components.

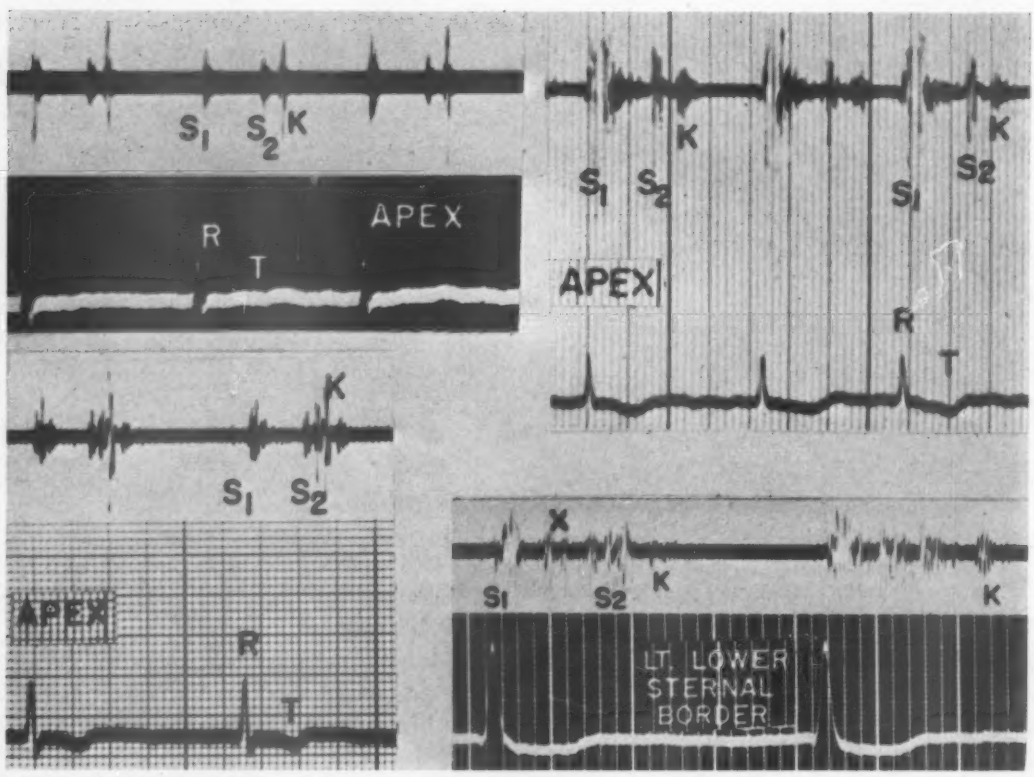

FIG. 6. Pericardial knock. Composite of four patients with constrictive pericarditis having pericardial knock sounds (K) in early diastole. First sound (S_1); second sound (S_2). Note systolic sounds (X) in right lower tracing.

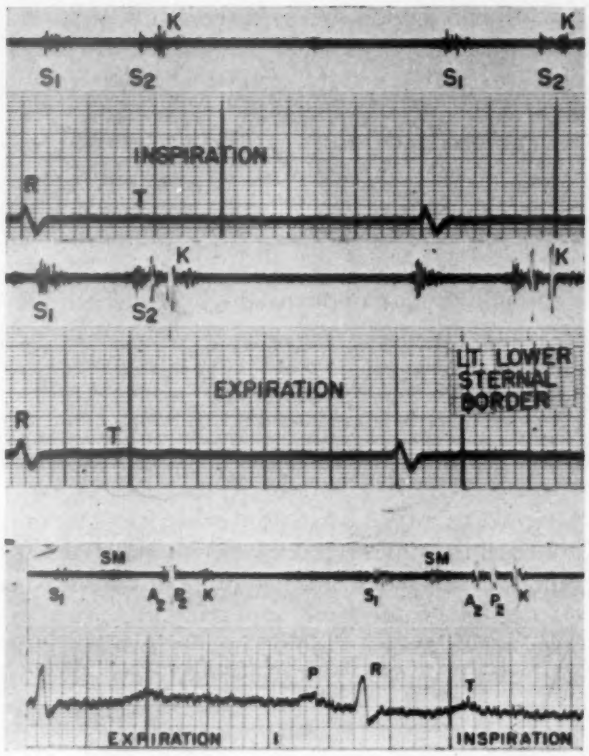

FIG. 7. Two patients with constrictive pericarditis. There is variation of knock sounds (K) with respiration. In the first patient (upper two strips) the knock sounds (K) decrease with inspiration. In the second patient (lower tracing) the knock sounds increase with inspiration. Normal splitting of second sound ($A_2 - P_2$).

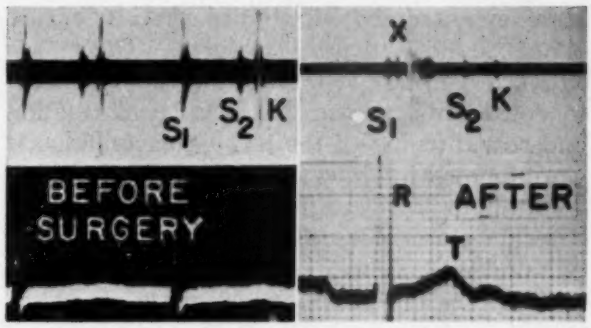

FIG. 8. Pericardial knock sound before and after surgery in a fifty-three year old woman incapacitated from constrictive pericarditis. Loud, single pericardial knock sound (K) before surgery. After successful operation, knock sound was faint, occurring later after second sound (S_2) than before surgery. Systolic sounds (X) had persisted for several years.

rub may be heard immediately after mitral valve surgery (Figs. 3 and 5), persist for hours or days but in itself is not cause for concern.

PERICARDIAL EFFUSION

Heart sounds (and murmurs, if present) may decrease significantly in the presence of pericardial effusion, particularly of large amounts of fluid. With slight or moderate amounts of pericardial fluid, sounds are frequently unaltered. In selected cases the effect of body position on heart sounds and murmurs has been useful in detecting the presence of pericardial fluid, eliminating the need for more specialized diagnostic procedures.[3] With the patient lying on his back, the intensity of heart sounds and murmurs is noted; with the stethoscope kept in the same area the patient then turns on his abdomen, propping himself up on his elbows. Normally heart sounds and murmurs remain the same or are slightly increased, while in some cases of pericardial effusion the heart sounds paradoxically become fainter. This observation has been of particular value in detecting moderate amounts of effusion when the roentgenogram and electrocardiogram are inconclusive. On the other hand, with small effusions there may be no significant decrease in sounds and with the largest effusions there may be little or no alteration of the sounds. If pleural effusion is also present, a false positive sign may be confusing, causing diminution in heart sounds coincident with the patient turning on his abdomen. In selected cases, however, particularly when other evidence is not of diagnostic value, the decrease in sounds and/or murmurs has proved useful, and is sometimes the first indication of the presence of pericardial fluid.

CONSTRICTIVE PERICARDITIS

The term "pericardial knock" is used to designate a sound occurring in early diastole (Figs. 6 to 8) and is commonly heard in patients with constrictive pericarditis.[4–6] It may occur whether calcification of the pericardium is present or not. This sound seems to be related to filling of the ventricles in diastole and is produced when the blood fills the ventricles during early diastole; the constricting pericardium acts as a restricting shell preventing the usual relaxation of the ventricles in diastole. The sound generally occurs slightly later than the opening snap of a tight mitral stenosis but earlier than the normal physiologic third heart sound or ventricular diastolic gallop. It is usually noted in patients with constrictive pericarditis and is often confused with an opening snap of mitral stenosis. Constrictive pericarditis is

sometimes confused with mitral stenosis because of this sound and other features. The classic rumble of mitral stenosis, however, is absent in constrictive pericarditis. Atrial fibrillation and straightening of the left cardiac silhouette can be noted in either; but if the possibility of constrictive pericarditis is considered, other clinical features will suffice to make the diagnosis. A sound in this phase of diastole should always alert one to the possibility of constrictive pericarditis and to search for its other features.

The sound of pericardial knock is variable (Fig. 6). It may be a loud single component, or of less intensity, of longer duration, or consist of several components. At times the variation is related to respiration (Fig. 7). After surgery for constrictive pericarditis the diastolic sound may persist but it often occurs at a later interval after the second sound (Fig. 8), consistent at times with a ventricular diastolic gallop or physiologic third heart sound. Whether this sound is related to residual pericardial adhesions or to the ventricular gallop associated with congestive heart failure or both is not settled at present. An element of myocardial failure can be present in a number of patients for a considerable time before there is significant clinical improvement. It is known that months or even a year may pass after surgery before the patient obtains demonstrable or maximum benefit.

Systolic sounds, presumably related to pericardial adhesions or pathologic changes in the pericardium, may be present before and/or after surgery (Figs. 6 [right lower tracing] and 8).

Summary

A friction rub characteristic of pericarditis is composed of several components, the typical friction rub having two or three. The first part (provided the rhythm is normal sinus) is related to atrial systole, resulting in a friction component in presystole. The second component is related to ventricular systole, producing a systolic friction rub. The third component generally occurs in the early to middle phase of ventricular diastole, apparently coincident with the time of rapid filling. Sometimes only two components are heard which may be related to atrial systole and ventricular systole. If the rhythm is irregular with atrial fibrillation (thereby having no atrial component), a friction rub having two parts is produced in ventricular systole and diastole. As a practical rule, one should hesitate to make a diagnosis of acute pericarditis after hearing only one friction component in systole, although occasionally it may represent an early finding of pericarditis with the diastolic component appearing subsequently. The auscultatory results in pericardial effusion and constrictive pericarditis are discussed.

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The Electrocardiogram in Pericarditis*

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THE ELECTROCARDIOGRAM is abnormal in many, perhaps in most, cases of clinically significant pericardial disease. Frequently the electrocardiographic abnormalities are characteristic of or strongly suggestive of pericarditis, but only rarely, if ever, are they in themselves diagnostic. Nor are such electrocardiographic changes present in all cases of pericardial disease, since none of them is due directly to involvement of the pericardial membranes *per se*.

The characteristic electrocardiographic abnormalities include:

1. *Displacement of the RS-T junction*, attributable to incomplete recovery (repolarization) of myocardial fibers subjacent to the epicardium—subepicardial injury. Junction displacement is observed only in cases of acute, or at least active pericarditis.

2. *Abnormalities of the T wave*, due to delay in recovery (repolarization) of subepicardial fibers of the myocardium. Such T wave abnormality, occurring for the most part in acute or active pericarditis but not rarely in chronic inactive disease, represents a lesser degree of subepicardial injury than that which leads to RS-T junction displacement—the so-called "ischemia" effect which in this instance is a misnomer.

3. *Low voltage* (*small amplitude*) of the waves and complexes due either to (a) altered transmission of the electric potentials of the heart to the body surface because of the interposition of pericardial fluid, or (b) diminution of the electromotive forces incident to the heart beat related to atrophy of the myocardium in cases of *concretio cordis*.

HISTORY

The electrocardiographic changes in pericardial disease were all well described during the decade between 1920 and 1930; by 1935 their genesis, diagnostic value and differentiation from similar changes due to myocardial ischemia and other types of myocardial disease were as well known and as clearly undertsood as they are today. Interestingly, it was during this fifteen year period that nearly all of the important diagnostic features of the electrocardiogram (except those relating to the cardiac arrhythmias, which were described earlier) were described and categorized. Much of this knowledge resulted from the investigations of American workers, all within two decades after the electrocardiogram was introduced into this country by Dr. Alfred E. Cohn.

In 1923 Oppenheimer and Mann[1] described low voltage of the electrocardiogram in cases of pericardial effusion and correctly attributed this abnormality to alteration of the conducting medium. They noted also that low voltage is not diagnostic of effusion, but might occur in "cases with myodegeneration." Further, they quite correctly warned that "fairly large effusions may fail to affect the voltage of the electrocardiogram appreciably in certain cases." Gazer[2] in 1924 noted low voltage and partial atrioventricular block in a case of pericardial effusion, "indicating a poor functional state of the heart muscle," a correct conclusion in their case.

Cohn and Swift[3] in 1924 reported that in some cases of rheumatic fever the "R-T period . . .lies higher or lower than in other curves," and that "the T wave alone may undergo . . .inversion." It seems likely that in some of their cases these changes were due to pericarditis, although no electrocardiograms were reproduced in their report. In 1927 Rothschild, Sacks and Libman,[4] in a consideration of the electrocardiogram in bacterial endocarditis and rheumatic fever, published records from two cases of rheumatic fever which present typical RS-T shifts of pericarditis, one of which is reproduced here (Fig. 1). Reid and Kenway[5] in 1928 reported that in eleven of twenty-six cases of rheumatic

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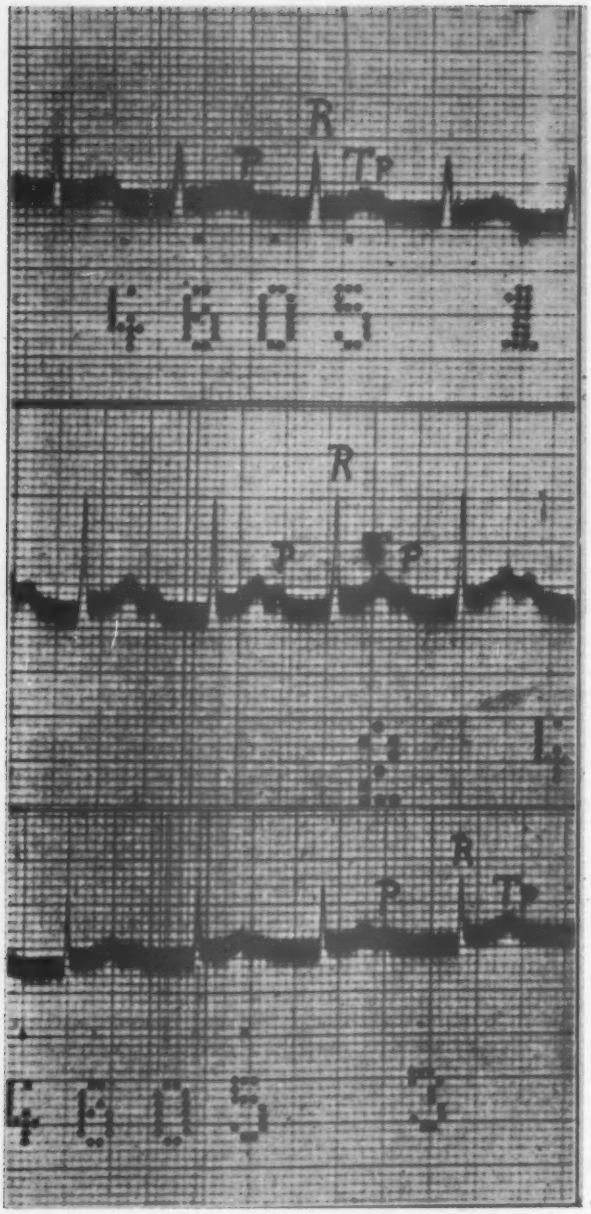

FIG. 1. Male patient, age twenty-four, with acute rheumatic fever. (From Rothschild, Sacks and Libman. *Am. Heart J.*, 2: 361, 1927.[4] Reproduced by permission of C. V. Mosby Co.)

carditis there was "absence of an isoelectric period between the end of the QRS complex and the . . .T wave," but none of their published records is typical of pericarditis.

In 1929 Porte and Pardee[6] reported on "the occurrence of the coronary T wave in rheumatic pericarditis" and published records of three cases showing T wave inversion in leads I and II; one of their records is reproduced here (Fig. 2). They believed, quite correctly, that "the T wave abnormality . . .is due to a complicating myocardial inflammatory reaction." Later in

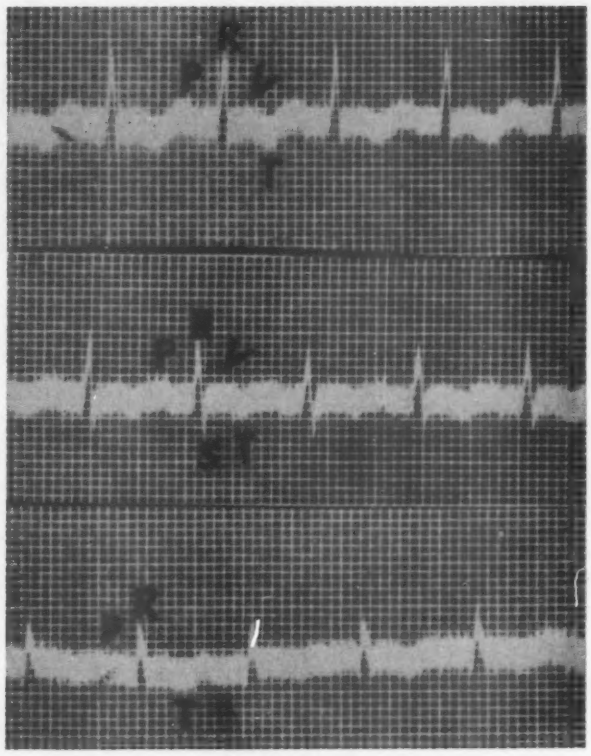

FIG. 2. Male patient, age twenty-seven, with rheumatic carditis. (From Porte and Pardee. *Am. Heart J.*, 4: 587, 1929.[6] Reproduced by permission of C. V. Mosby Co.)

the same year Scott, Feil and Katz[7] reported upward RS-T deviation in three cases of pericardial effusion, in one of which a friction rub was present (Fig. 3). This may be the first report correlating RS-T junction displacement with acute pericardial disease. Katz, Feil and Scott[8] noted similar changes in experimental pericardial effusion, as well as T wave inversion.

In 1931 Purks[9] reported a case of pneumococcal pericarditis in which there was upward displacement of the RS-T junction in leads I and II (Fig. 4); significantly, he stated that "with any case of pneumococcic pericarditis there is involvement of the myocardium for a depth of one or two millimeters. The occurrence of the T wave changes could be explained on this basis." Purks may have been the first to recognize the role of subepicardial injury in the genesis of the electrocardiographic changes in pericarditis.

During the late 1920's and early 1930's several investigators[10–14] called attention to the electrocardiographic changes in pericardial disease and compared these to the changes noted in coronary disease and other conditions affecting the myocardium. However, it remained for Herrmann and Schwab,[15–17] on the basis of animal experi-

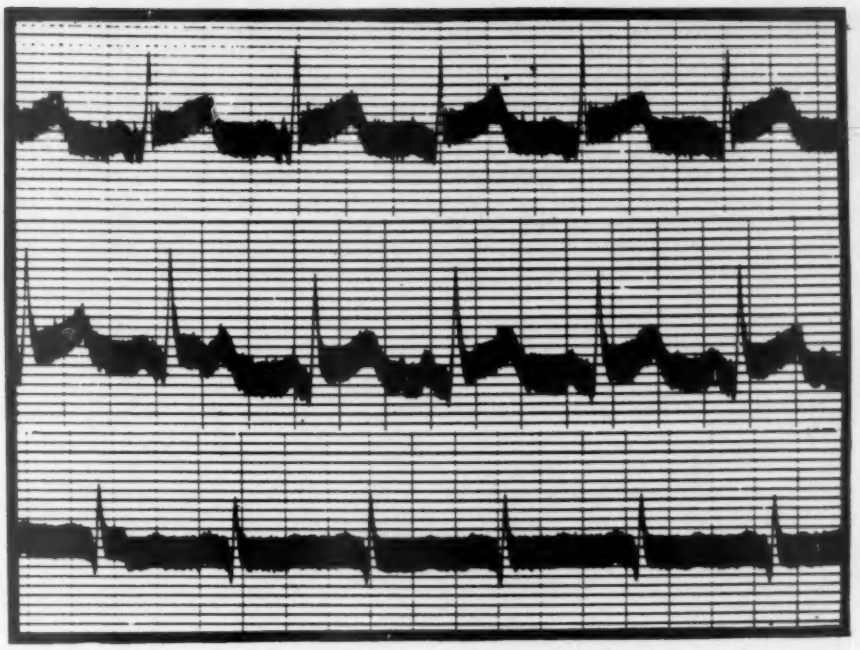

FIG. 3. (From Scott, Feil and Katz. *Am. Heart J.*, 5: 73, 1929.[7] Reproduced by permission of C. V. Mosby Co.) Authors' legend states: "Three leads from a case of purulent pericarditis with effusion. Note the high take-off of the S-T segment in leads I and II which merges with the T wave."

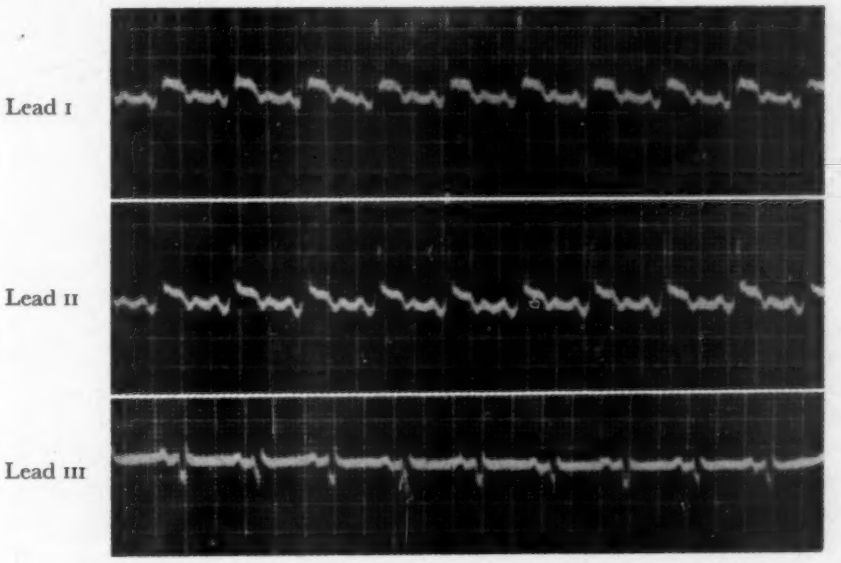

FIG. 4. A case of pneumococcal pericarditis. Leads I and II show the elevated plateau-like R-T inteval and lead III a deep S wave and slurring of the QRS (From Purks. *South. M. J.*, 24: 1032, 1931.[9] Reproduced by permission of the Southern Medical Association.)

ments, careful clinical observation and a complete review of the literature up to 1934, to describe the changes meticulously and to develop fully their differential diagnostic possibilities.

ACUTE FIBRINOUS PERICARDITIS

In typical cases the earliest electrocardiographic sign is displacement of the RS-T segment, as follows:

1. Upward in all three of the Einthoven leads, or in I and II only with no displacement in lead III. In the former case the deviation is necessarily greatest in lead II while in the latter case the shifts are of the same magnitude in I and II.

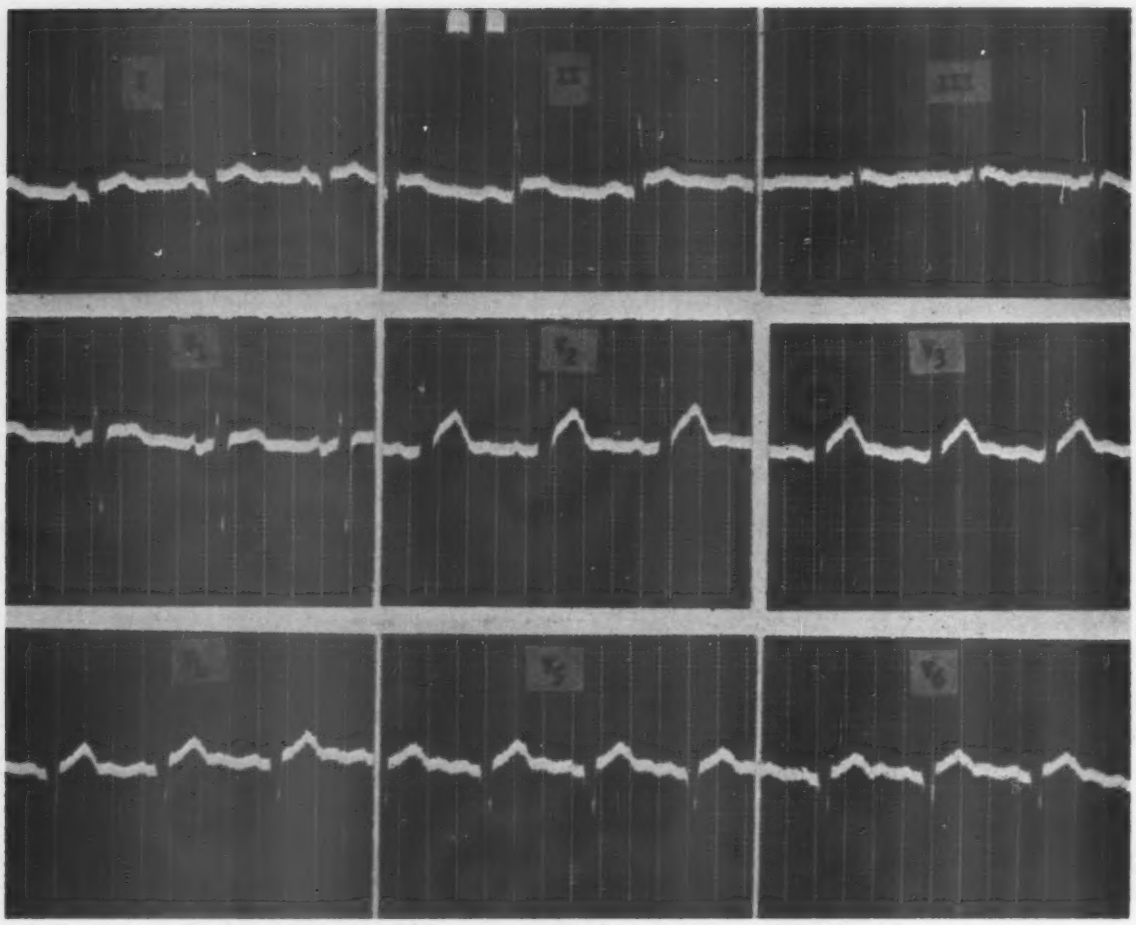

FIG. 5. Acute pericarditis ("idiopathic") in a patient with left ventricular hypertrophy.

2. Upward in all of the Wilson precordial leads except V_1 in which as a rule no displacement occurs. The shift is usually maximal in V_2 and V_3, or in V_2, V_3 and V_4.

3. Downward in aVR of the Goldberger leads, upward in aVF or aVL or both. In an occasional case the displacement is upward in aVF and downward in aVL (*vide infra*).

Characteristically, in early cases T waves of normal form evolve from the elevated RS-T segments; the upstroke of the T remains distinct from the RS-T segment, imparting an upward concavity to this portion of the record (Figs. 5 and 6).

Later as the process subsides or becomes less acute, the RS-T displacements diminish and finally disappear. The T waves may remain normal during this phase, so that with return of the RS-T segments to the base line no abnormality of the electrocardiogram remains. More often and more typically, the T waves diminish progressively in amplitude and finally invert (Fig. 7); in stages of this evolution a plus-minus T wave, with upward bowing of the RS-T segment, may be recorded. With the passage of weeks or months the T waves become upright and of normal amplitude in most cases (Figs. 8 and 9), but permanent inversion or diminished amplitude is not a rare sequel (Fig. 10).

T inversion, of course, tends to occur in leads of former upward RS-T displacement: in I, II and III or I and II; in V_2 to V_6; in aVL and aVF.

Not uncommonly acute pericarditis is manifested electrocardiographically only by lowering or inversion of the T waves, there being no RS-T displacements. Again, in some cases with typical symptoms and physical signs the electrocardiogram remains normal. Rarely, reciprocal RS-T displacements in leads I and III may be recorded (Fig. 11). Finally, it should be noted that RS-T displacements and/or T wave changes of the same order and magnitude as those observed in pericarditis may be recorded in healthy persons (Fig. 12), in cases of pneu-

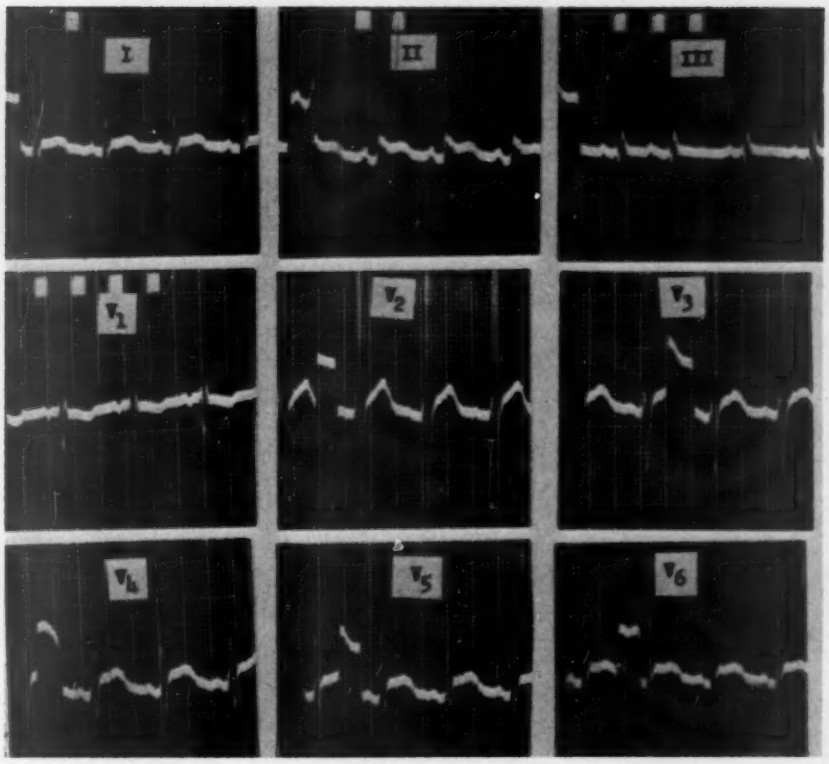

FIG. 6. Acute pericarditis due to Escherichia coli, April 22, 1958.

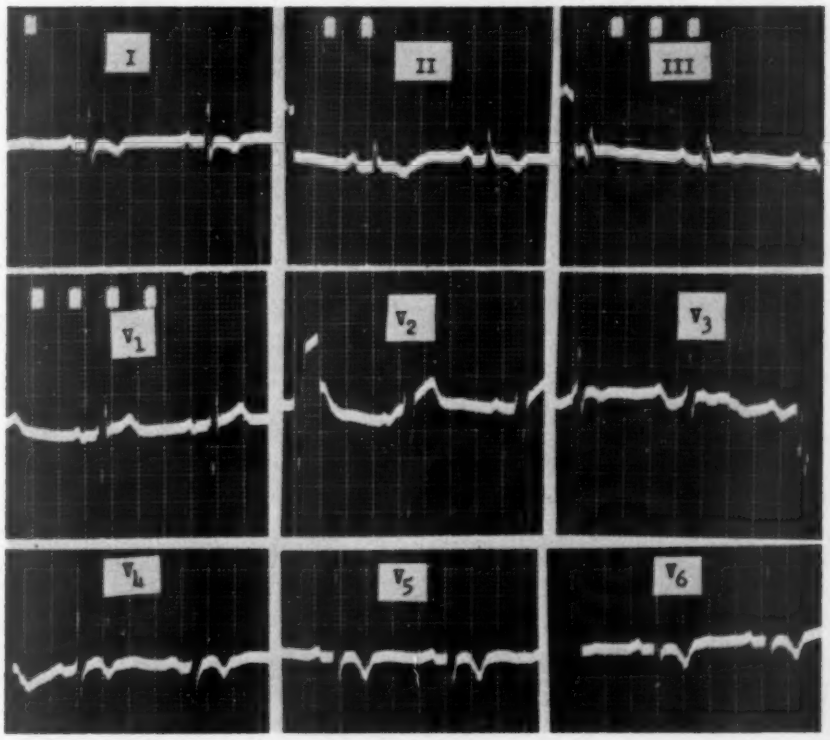

FIG. 7. Subacute or healing pericarditis; same case as shown in Figure 6; May 23, 1958.

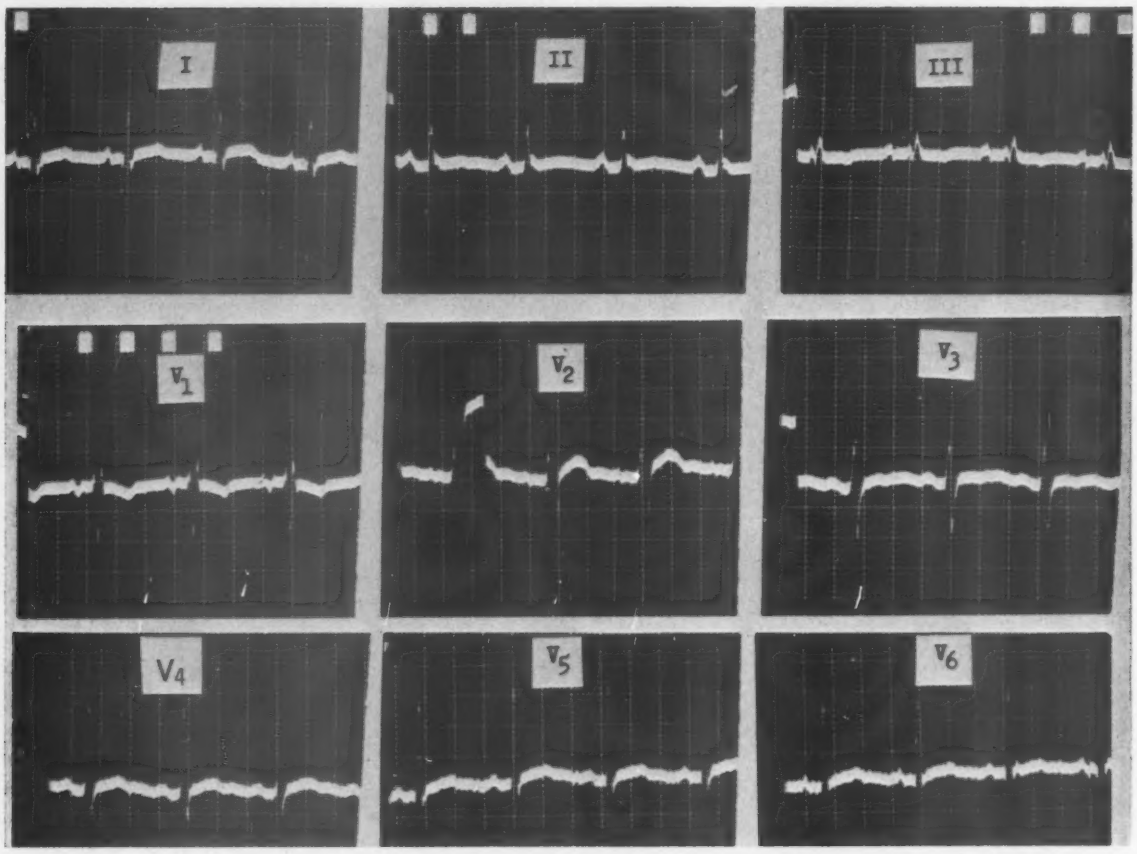

FIG. 8. Healed or healing pericarditis; same case as shown in Figures 6 and 7; July 1, 1958.

monia,[18] in myocardial ischemia, in myocarditis and other conditions affecting the myocardium.

Genesis of the Electrocardiographic Changes: It is probable that in most cases of fibrinous pericarditis which lead to changes in the electrocardiogram and in all cases which are manifest by typical changes, the process is diffuse, involving most or all of the epicardium. The net electrical effects of subepicardial injury as projected onto the frontal plane are therefore directed along a line between the valvular orifices and the region of the apex; in other words, the effects of injury in the region of the apex predominate. The "axis of injury," in the stage of RS-T displacement, points downward and to the left, its exact direction varying with the position of the heart. Figure 13 should suffice to explain the RS-T displacements of the extremity leads in typical cases.

Unusual positions of the heart may explain some of the less common distributions of the shifts among the limb leads: for example, in a vertical-apex back heart, the deviation might be downward in aVL, while in a markedly horizontal heart with counterclockwise rotation, reciprocal shifts might be recorded (up in I, down in III) (Fig. 14). Uncommon distribution of displacements might be due in other cases to more severe subepicardial injury in one region or another or to localized pericarditis.

The upward RS-T displacement in leads V_2 to V_6 is, of course, related to the proximity of the precordial electrodes to the anterior surface of the ventricles, and the usual absence of a shift in V_1 to the fact that in this lead the electrode faces the surface of the right atrium.

The distribution of T wave inversion can be correlated with the same factors which govern the distribution of RS-T shifts. The inversion is probably due to delay in recovery of injured subepicardial fibers, so that the predominant direction of the recovery process is from endocardium to epicardium, the reverse of normal. Again, events occurring in the region of the apex predominate in the projection of the electrical effects onto the frontal plane, so that the axis of the T wave comes to point upward and to the right.

In the cases which are manifest only by inversion or lowering of the T waves it is likely that either the subepicardial injury is not

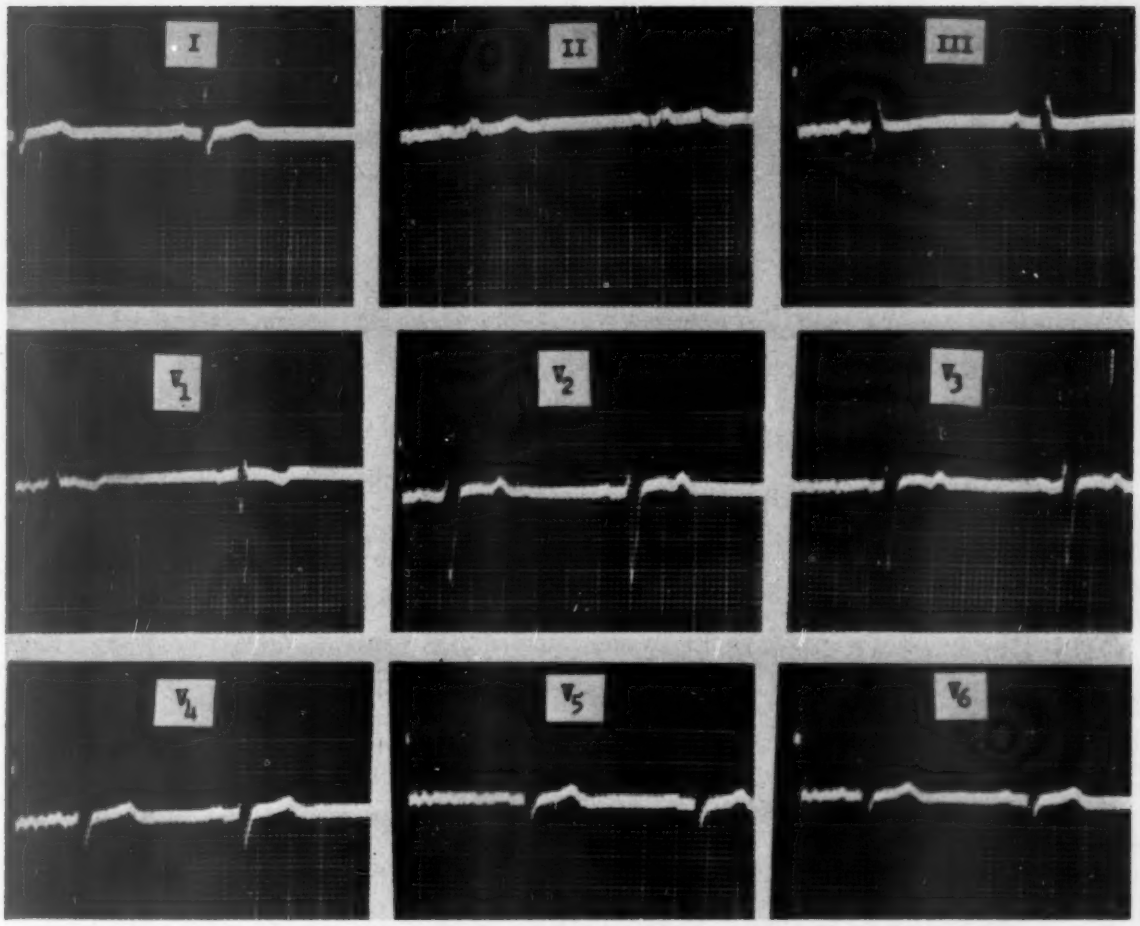

FIG. 9. Healed pericarditis; same case as shown in Figures 6 and 8; March 1, 1959.

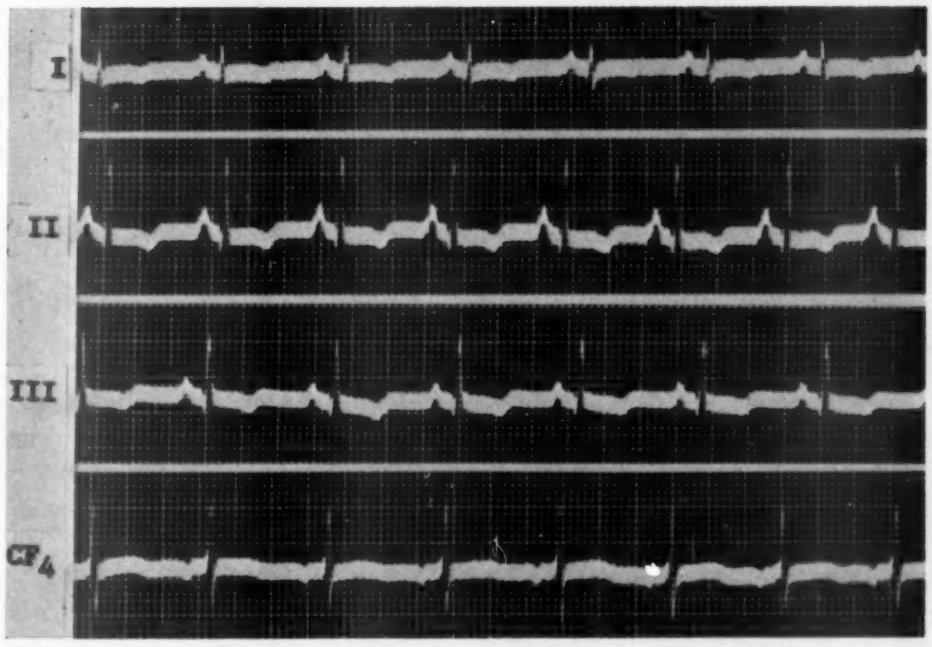

FIG. 10. Persistent T wave inversion twelve months after recovery from pericarditis with effusion; etiologic factor undetermined.

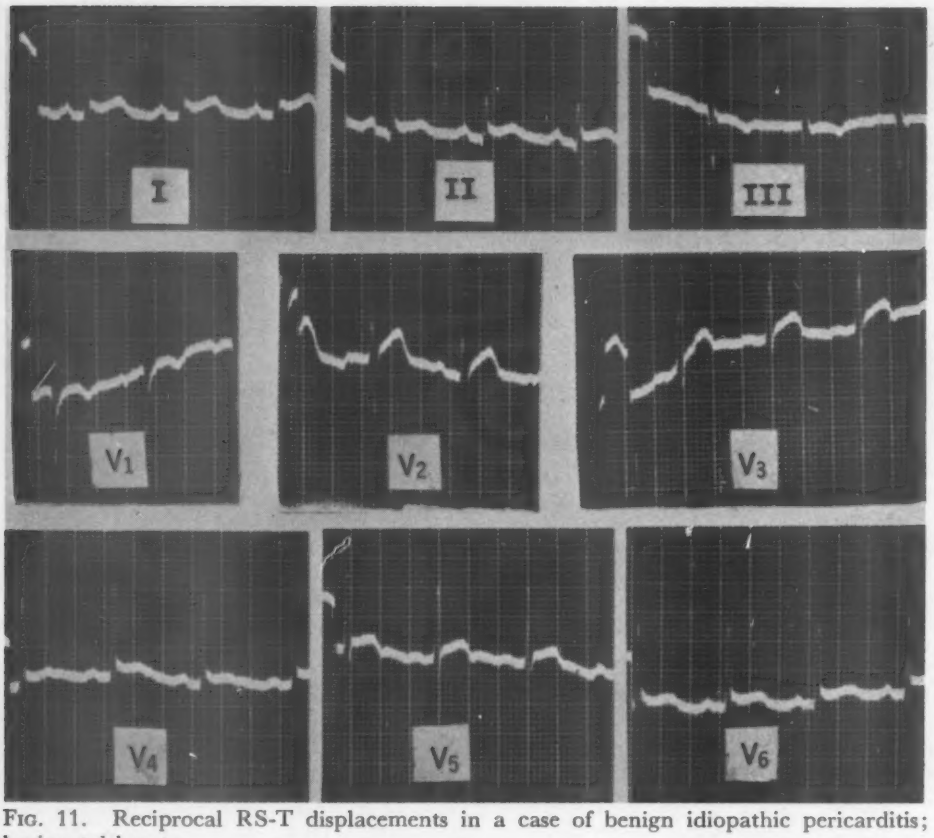

FIG. 11. Reciprocal RS-T displacements in a case of benign idiopathic pericarditis; horizontal heart.

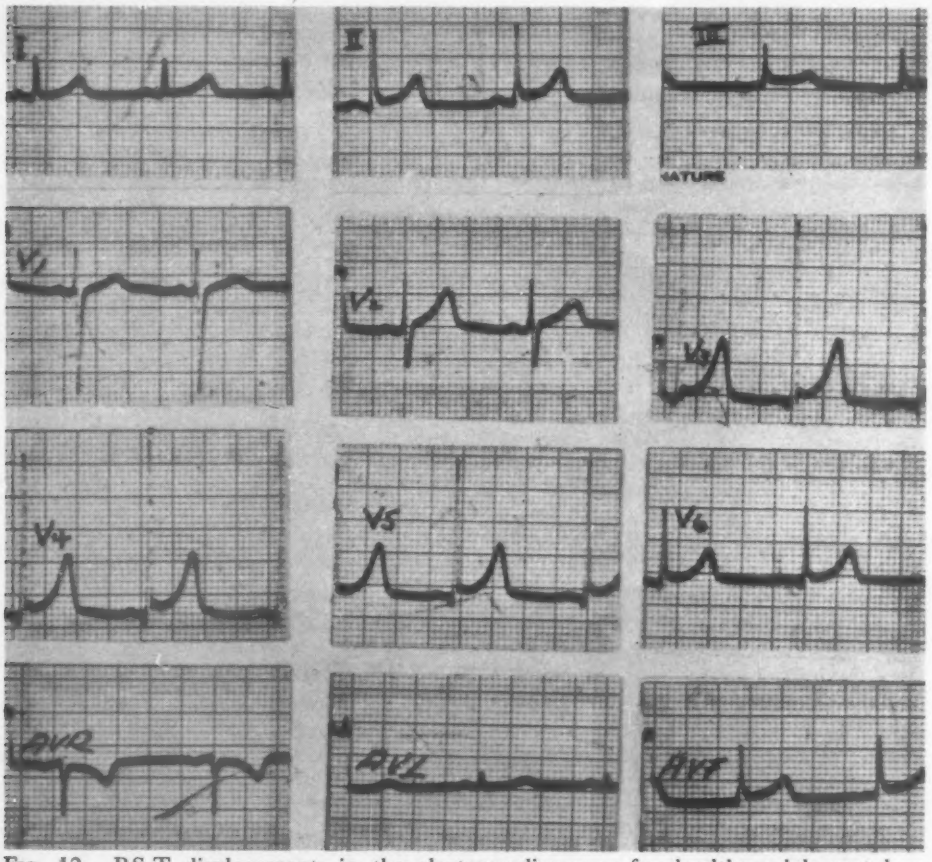

FIG. 12. RS-T displacements in the electrocardiogram of a healthy adolescent boy.

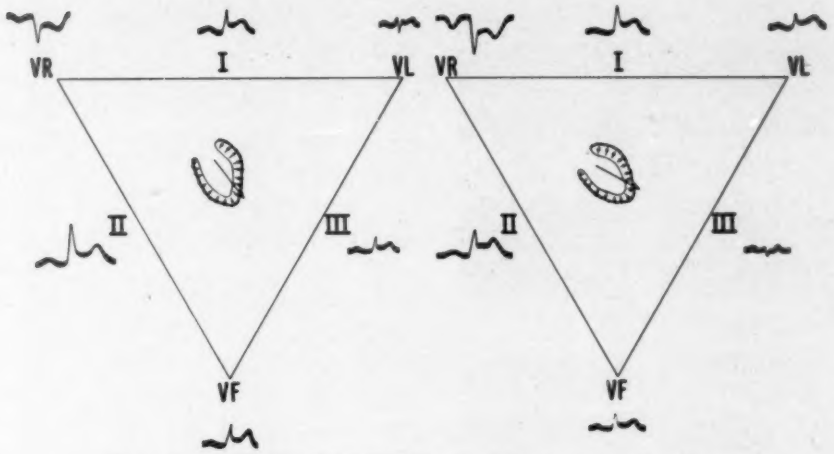

FIG. 13. Genesis of RS-T shifts in typical cases. See text.

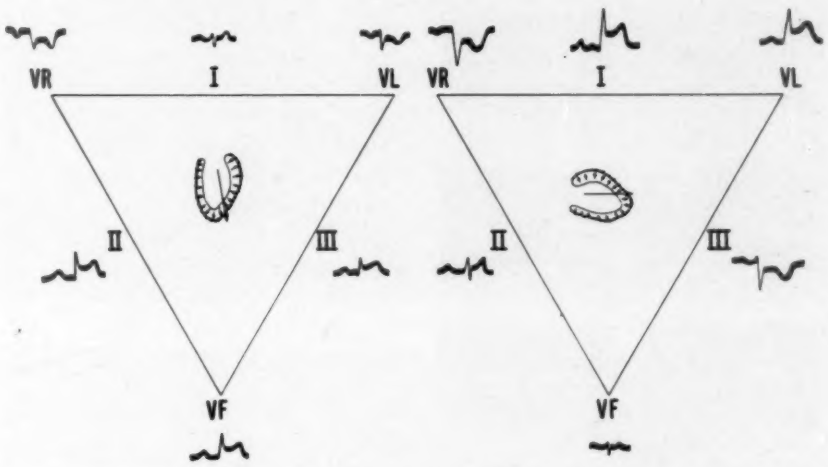

FIG. 14. Genesis of atypical RS-T displacements in pericarditis. See text.

sufficiently severe to prevent complete recovery of polarization, but only to alter its order; or that the injury has partially subsided by the time the first electrocardiogram is recorded.

It is to be noted that the genesis of the RS-T and T abnormalities encountered in fibrinous pericarditis differs in no way from that of changes in the terminal portion of the ventricular complex in cases of infarction, ischemia, myocarditis, etc.; it is, therefore, not surprising that on occasion other conditions may be characterized by changes identical with those seen in pericarditis.

The nature of the RS-T shifts which occur occasionally in pneumonia is not clear. In a case of ours which came to autopsy, in which the electrocardiogram showed RS-T shifts typical of pericarditis, there was an early paramediastinal empyema on the left side adjacent to the pericardium but no pericarditis. In this case it is possible that superficial fibers of the myocardium were "injured" because of proximity to the inflamed pleura, but in Schearer's case[18] (Fig. 15) the electrocardiographic changes occurred in a case of uncomplicated pneumonia involving only the right upper lobe; in this patient there was a pleural rub but no signs of pericarditis.

Differential Diagnosis: Fibrinous pericarditis cannot be recognized positively by the electrocardiogram although in most cases the typical changes described earlier are recorded. Typical serial changes may enable the electrocardiographer to be almost certain of his diagnosis, but in a single record signs "typical" of pericarditis may be encountered in normal hearts (Fig. 12), in early or impending infarction, in myocarditis and in other conditions.

The most frequent problem is the differentiation between pericarditis on the one hand and injury due to ischemia on the other, in the absence of changes in the QRS which are diagnostic of infarction. In such cases the following signs (most of which were pointed out

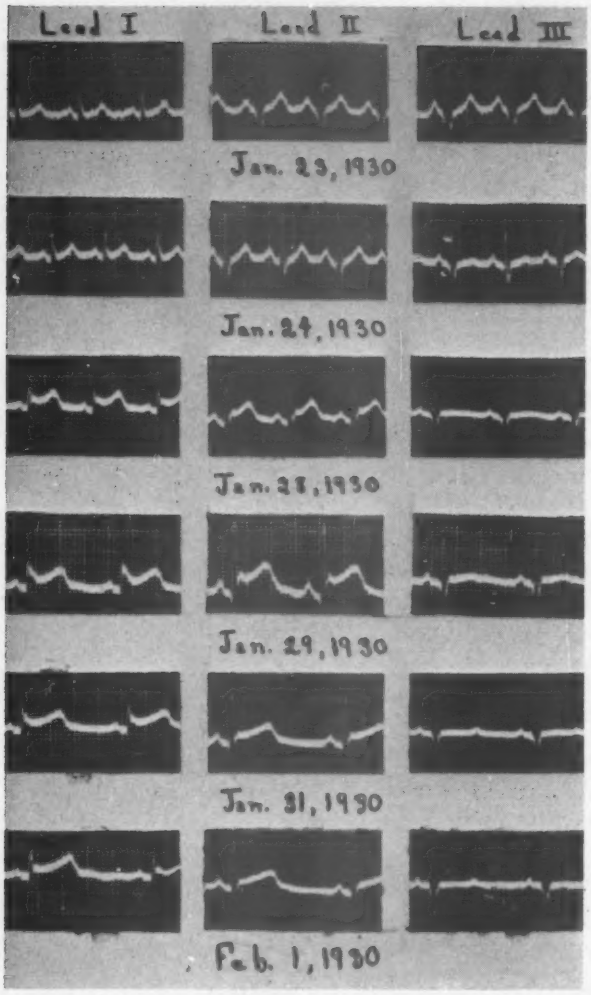

FIG. 15. Changes typical of pericarditis in a case of right upper lobe pneumonia. (From Shearer. *Am. Heart J.*, 5: 801, 1930.[18] Reproduced by permission of the C. V. Mosby Co.)

by Herrmann and Schwab[15–17] a quarter of a century ago) are suggestive of ischemia rather than pericarditis: (1) Reciprocal RS-T displacements in the Einthoven leads; (2) marked RS-T displacements, more than 4 or 5 mm.; (3) fusion of the RS-T segment and T wave into a single complex, forming a "monophasic" curve; (4) in the early stage of T inversion, pronounced upward bowing of the RS-T segment—the Pardee T wave; (5) very deep T wave inversion.

Not very rarely exceptions to (2) and (5) will be encountered, in that rather marked RS-T shifts or deeply inverted T waves will be recorded (Fig. 16) in cases of pericarditis. Exceptions to (1), (3) and (4) are rare.

Pericardial Effusion

In many cases of pericardial effusion due to inflammation or to neoplasm the electrocardiographic changes of fibrinous pericarditis (which has usually preceded effusion) are recorded. In some cases, but not in nearly all, the amplitudes of all waves and complexes in extremity leads are diminished, but such diminution is less likely to occur in precordial leads (Fig. 17). In other cases and in transudative effusions one encounters only low voltage waves and complexes. In a considerable number of effusions, even large ones, amplitudes are not abnormally small.

In pericardial effusion low voltage is, as is well known, related to alteration of the electric fields set up in the heart by the layer of fluid which surrounds it; identical changes may occur in pleural effusion and in edema due to congestive heart failure or other conditions. The low voltage of fluid accumulation is not often distinguishable electrocardiographically from that due to metabolic disorders of the myocardium (hypothyroidism, for example, in which, incidentally, pericardial effusion may occur), and may closely resemble that due to diffuse myocardial disease caused by coronary atherosclerosis, amyloidosis, progressive systemic sclerosis, or neoplasm. All in all, the electrocardiogram plays a minor role in the diagnosis of pericardial effusion.

Chronic Pericarditis

As stated earlier, abnormalities of the T wave may persist following recovery from fibrinous pericarditis, such persistence probably being due to the development of subepicardial fibrosis. Undoubtedly, ancient healed pericarditis is responsible for T wave abnormalities which have been ascribed to ischemia or some other cause.

The electrocardiogram is abnormal in most but not in all cases of chronic constrictive pericarditis. The characteristic abnormality is low voltage of the QRS complex and the T wave, with not infrequent shallow inversion of the T in lead I or I and II, and/or in one or more of the precordial leads (Fig. 18). The amplitude of the P wave also may be diminished. Atrial fibrillation is common. The changes are undoubtedly attributable to subepicardial fibrosis and myocardial atrophy. Perhaps the frequent occurrence of atrial fibrillation is related, as it is in atrioventricular valve stenosis, to prolonged elevation of atrial pressures.

Although the changes are characteristic, they are not diagnostic as would be expected from what is known of their genesis. In most

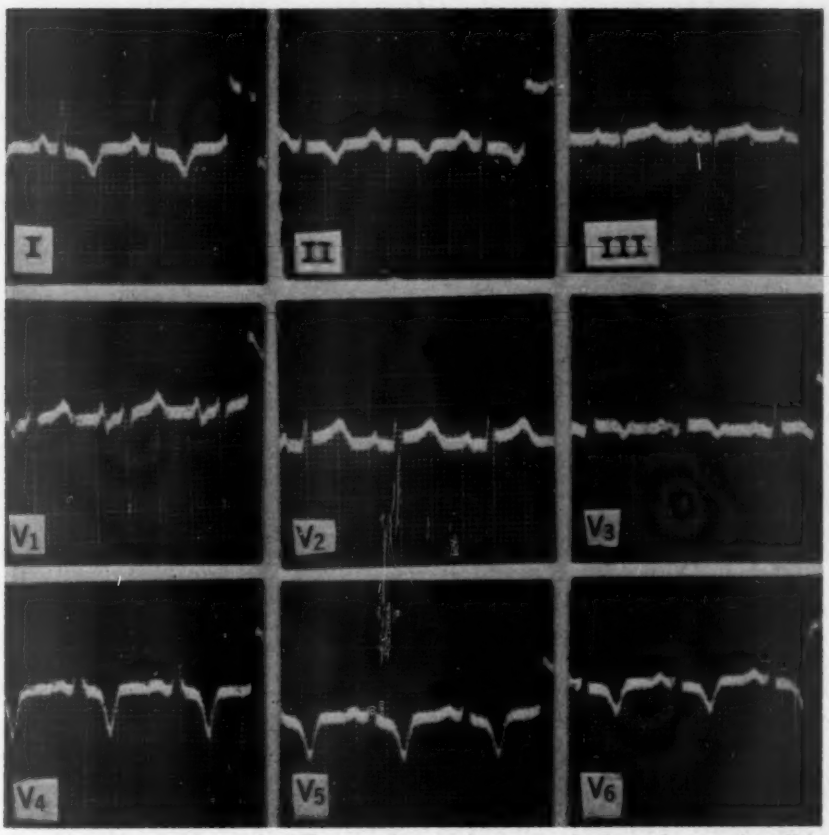

FIG. 16. Unusually marked T wave changes in a case of tuberculous pericarditis.

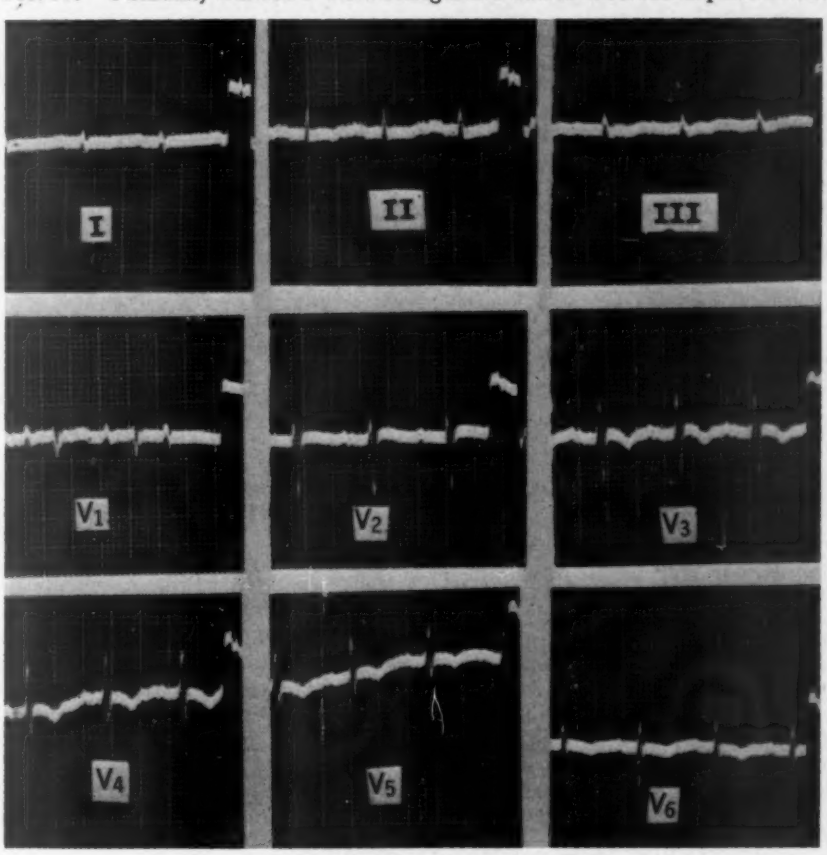

FIG. 17. Tuberculous pericardial effusion.

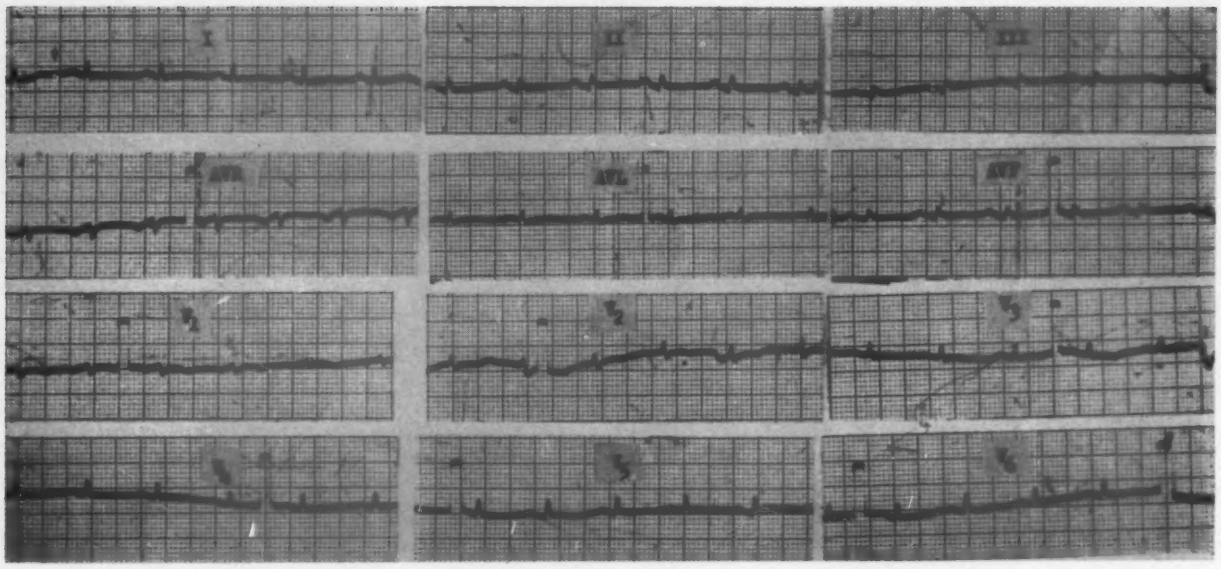

FIG. 18. Constrictive pericarditis. Note low voltage of ventricular waves.

cases the electrocardiographic abnormalities are indistinguishable from those due to other conditions which are characterized by low voltage waves and complexes.

CONCLUSIONS

The electrocardiogram is altered in most cases of clinically significant pericardial disease. Although the electrocardiographic changes are usually characteristic, they are almost never absolutely diagnostic, although in cases of fibrinous pericarditis serial electrocardiograms may be very nearly so. In pericardial effusion and *concretio cordis* the electrocardiogram often makes the clinical picture more complete but rarely renders it more clear.

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Roentgenography of Pericardial Disease*

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ROENTGENOGRAPHY contributes significantly to the diagnosis of pericardial disease. The enlarging poorly pulsating cardiac silhouette may be the initial sign of pericardial effusion. Similarly, the discovery of pericardial calcifications may be the clue that leads to the diagnosis of constrictive pericarditis. Even though the motion, size and shape of the cardiac silhouette is discernible roentgenographically, it may still be impossible to differentiate a pericardial effusion from a dilated and enlarged heart (Fig. 1). Happily, angiocardiography by delineating the cardiac chambers differentiates such hearts (Fig. 1B and C) from pericardial effusions. Angiocardiography also differentiates adjacent mediastinal masses from the cardiovascular system. Right heart catheterization by defining the limits of the right atrium, while of some value in the diagnosis of pericardial effusion, is not entirely reliable because the left heart chambers cannot be visualized so that a mediastinal mass adjacent to the right heart may give similar findings.

Angiocardiography has not only proved to be valuable in the diagnosis of pericardial disease but it has also aided the understanding of the way pericardial fluid accumulates. In this review the value of angiocardiography for diagnosis of constrictive pericarditis and intrapericardial tumor will also be discussed.

PERICARDIAL EFFUSION

The size of the cardiac silhouette in pericarditis with effusion depends upon the amount of pericardial fluid and on the bulk of the heart. The most reliable and earliest sign of pericardial effusion is enlargement of the cardiac silhouette in serial roentgenograms. Normally, the peri-

A B C

FIG. 1. Cardiac dilatation and chronic heart failure (due to long-standing atrial flutter) simulating pericardial effusion in a fifty-two year old woman without heart murmurs. Verification of angiocardiographic findings secured by autopsy three months later. A, frontal teleroentgenogram showing marked enlargement of a poorly pulsating heart. B, frontal teleangiocardiogram shows the superior vena cava (SVC) to be widened; the right atrium (RA) is markedly dilated, and the right ventricle (RV) is huge. C, when the left heart is opacified (eighteen seconds after beginning of injection of the contrast material), there is a moderately enlarged left atrium (LA), the left ventricle (LV) is markedly dilated while the aorta (AO) appears to be normal in size.

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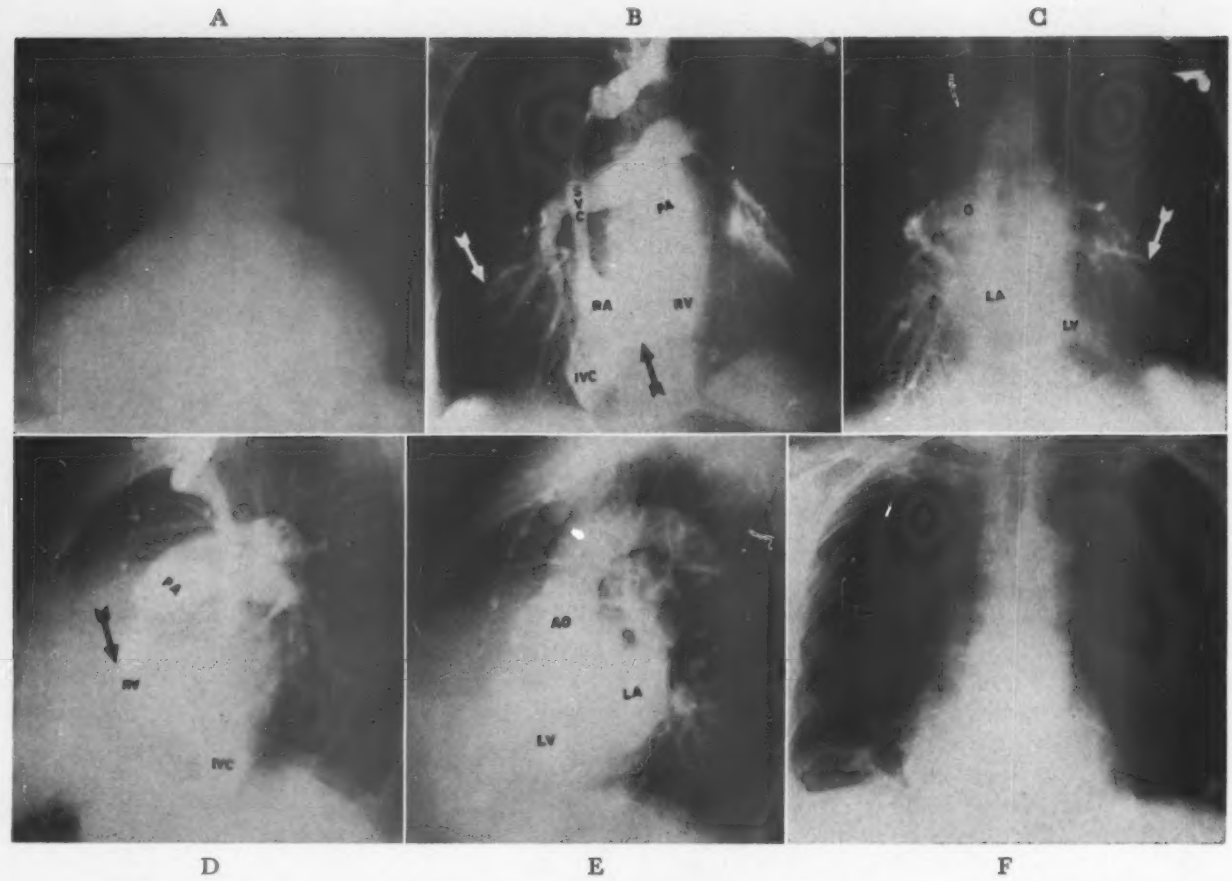

FIG. 2. Massive chronic idiopathic pericarditis with effusion in a sixty-five year old woman. A, frontal teleroentgenogram showing a huge cardiac silhouette, more marked along the right side. B, frontal teleangiocardiogram reveals the pericardial fluid (white arrow) to extend well beyond the opacified right atrium (RA). Lower black arrow points to the infracardiac pericardial effusion. SVC is the superior vena cava, IVC is the inferior vena cava, RV is the right ventricle and PA is the pulmonary artery. C, when the left heart structures are filled (LA is left atrium; LV, the left ventricle and AO the aorta), the pericardial effusion (arrow) is seen to extend well beyond the opacified left ventricle. D, lateral teleangiocardiogram of the right heart structures shows the pericardial fluid to be retrosternal and anterior to the opacified right ventricle (RV and arrow). E, lateral teleangiocardiogram of the left heart structures also shows the retrosternal collection of pericardial fluid. Note that the left atrium (LA) is not surrounded by fluid F, frontal teleroentgenogram, following pericardiostomy and drainage, shows the normal size and contour of the heart. (Republished with permission of *Surg. Gynec. & Obst.*[11])

cardial sac contains 15 to 30 cc. of fluid. It has been estimated that at least 250 cc. of fluid is necessary to cause a recognizable change in the cardiac shadow. Fluid first accumulates in the most dependent portion of the pericardium and then retrosternally (the area of least resistance).[1] The pyriform (water bottle) shape in the erect position may become more globular in the horizontal position due to gravitational effect. The length of the cardiac silhouette increases more rapidly than its transverse diameter. Straightening of the normal contours, especially the left, also aids in the diagnosis of pericardial effusion.[2] The superior mediastinum on the right may, in some instances, such as in cardiac tamponade, be widened by an enlarged superior vena cava; usually, cardiac pulsations are diminished or absent. Change in size of the heart does not occur with the Müller or Valsalva maneuvers in pericardial effusions in contradistinction to dilated hearts.[3] Also, the right cardiohepatic angle often becomes more acute with massive effusions.

These roentgen signs, while helpful, rarely permit the definitive diagnosis of pericardial effusions. This is well summarized by Kern et al.[4] in their discussion of the pitfalls in the roentgen diagnosis of percardial effusion in myxedema. Angiocardiography, on the other hand, conclusively differentiates between a pericardial effusion and cardiac dilatation.[2,5] Opacification of the cardiac chambers estab-

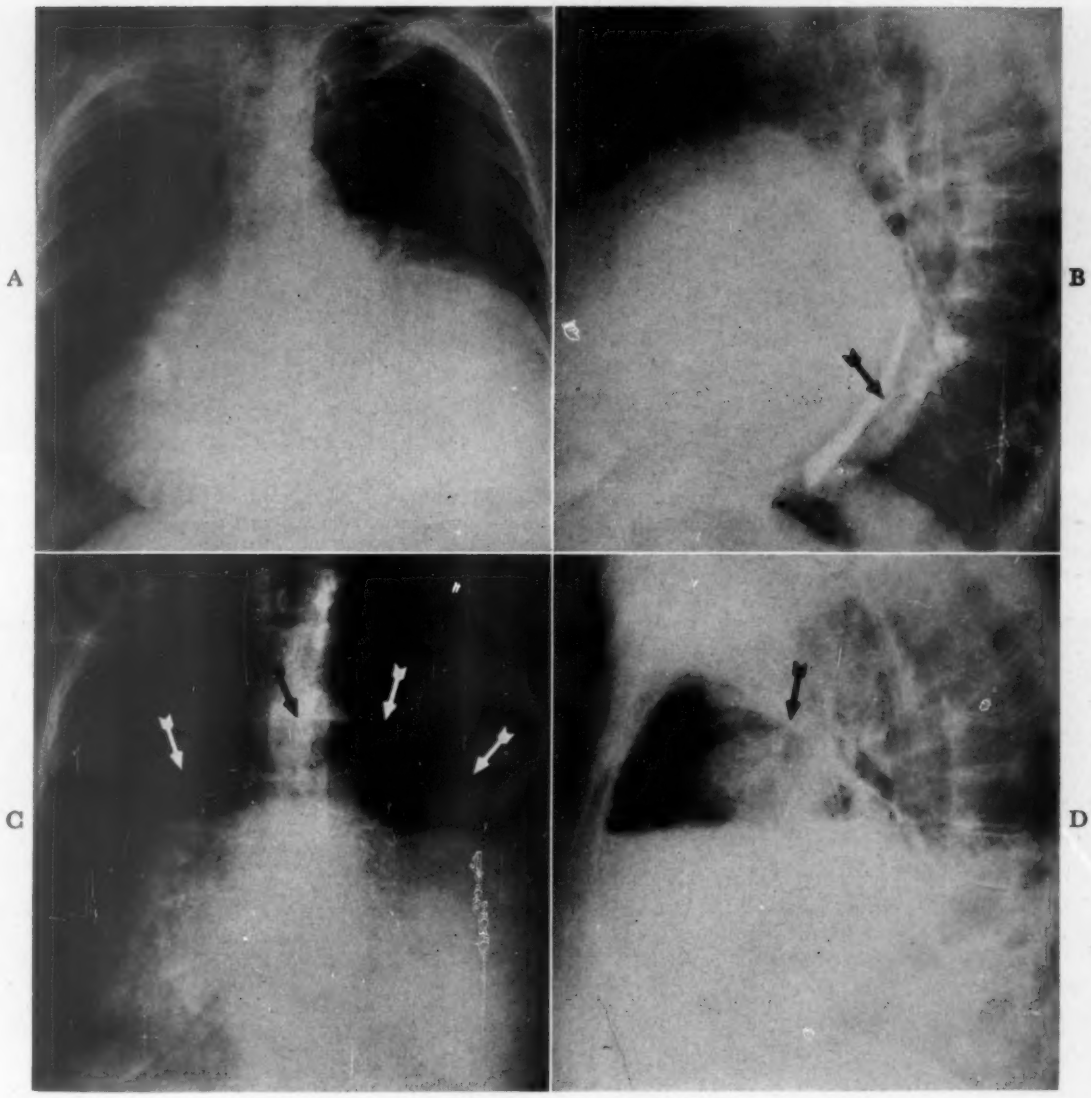

FIG. 3. Massive idiopathic recurrent pericardial effusion in a sixty-seven year old woman. A, frontal teleroentgenogram showing a huge cardiac silhouette. B, lateral esophagram shows the retrosternal collection of the pericardial fluid. Beyond the esophagus (arrow) there is pericardial fluid due to distention of the lateral pericardial pouches. C, frontal roentgenogram shows a pneumopericardium with the fluid level of the effusion and the distended pericardium above (arrows). D, lateral roentgenogram reveals that the pneumopericardium is anterior, clearly demonstrating the anterior location of pericardial effusions. (Republished with permission of *Surg. Gynec. & Obst.*[11])

lishes their size. From this, estimation of the size of the walls of the chambers may be made. Normally, the wall of the right atrium measures between 1 to 3 mm., the right ventricle 3 to 5 mm. and the left ventricle 10 mm. Hypertrophied ventricles rarely exceed 20 mm. Accordingly, a soft tissue density greater than the above, especially if it surrounds the heart in frontal view, is most likely to be due to pericardial fluid. Pericardial thickening due to chronic pericarditis is usually of moderate degree (5 mm.); whereas pericardial fluids may measure as much as 40 mm.[2,5,6]

Angiocardiography in Diagnosis of Pericardial Effusions: Figure 2 shows the conventional roentgenograms and angiocardiograms taken in the erect position of a sixty-nine year old woman with a massive pericardial effusion of long standing. The frontal view shows the classic appearance of pericardial fluid surrounding the heart (Fig. 2B and C). In the lateral views (Fig. 2D and E) the pericardial fluid is entirely anterior and does not surround the posterior part of the heart. The position of the cardiac chambers and great blood vessels within the distended pericardium in this case was also verified

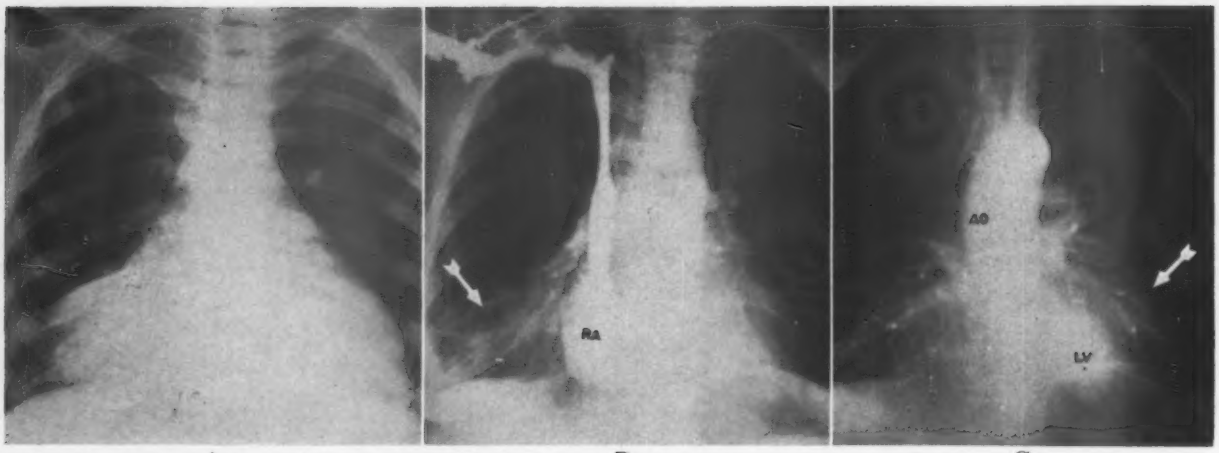

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FIG. 4. Pericardial effusion (infectious) in a thirty-six year old woman. A, frontal teleroentgenogram shows an enlarged (chiefly the right) cardiac silhouette. B, frontal angiocardiogram clearly shows the pericardial fluid (arrow) lateral to the opacified right atrium (RA). C, when the left cardiac chambers are filled, the pericardial fluid is seen to surround the heart. (Republished with permission of *Am. J. Roentgenol.*[2])

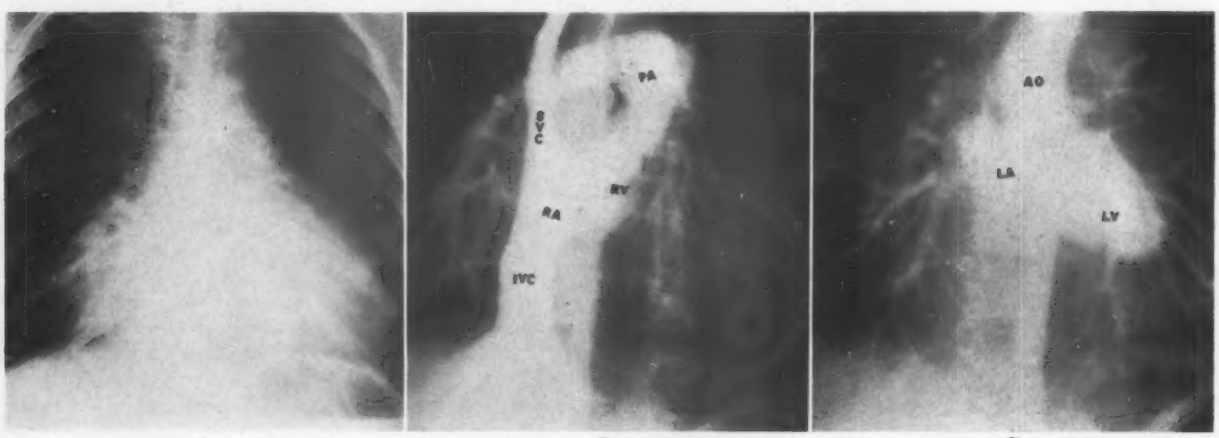

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FIG. 5. Chronic massive chylous pericardial effusion in an eleven year old boy. A, frontal teleroentgenogram showing a huge cardiac shadow. B, frontal angiocardiogram reveals the huge pericardial effusion laterally and infracardiacally. C, when the left heart structures are opacified, the remainder of the heart is seen to be surrounded by fluid. (Reproduced with permission of *Surg. Gynec. & Obst.*[11])

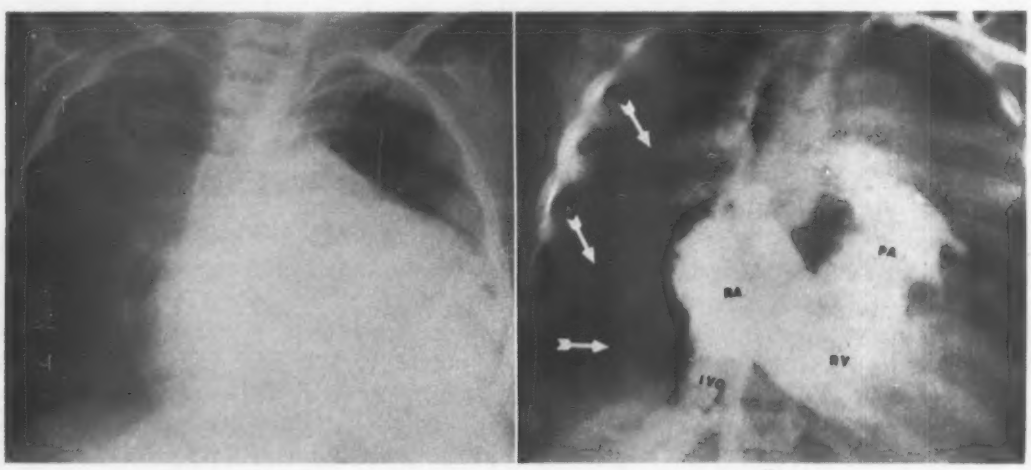

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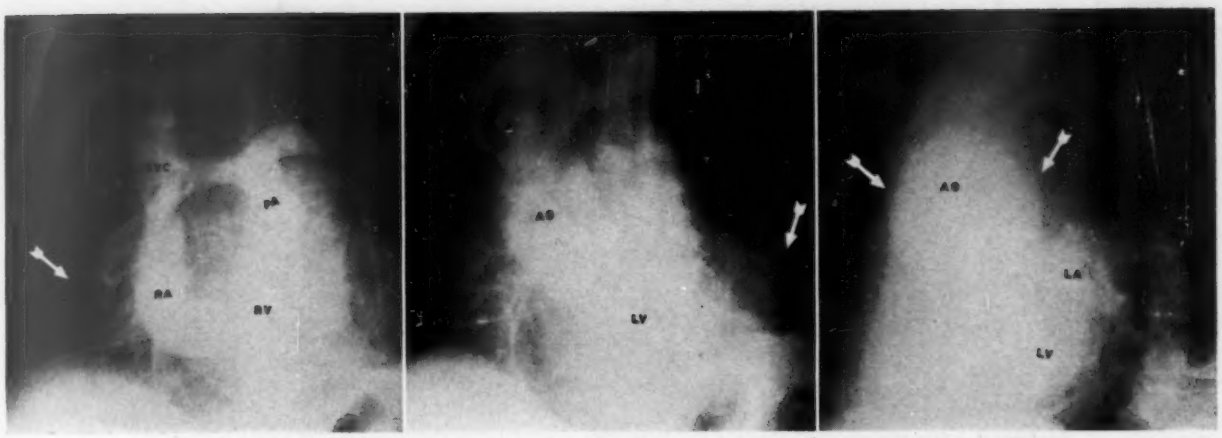
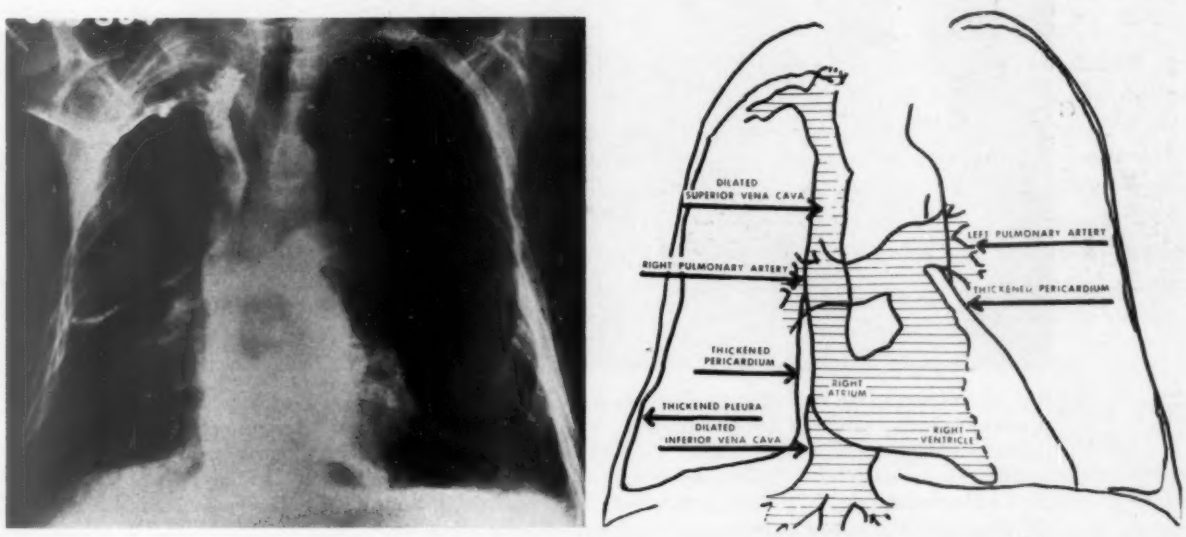
FIG. 6. Huge cardiac silhouette due to heart failure, myocarditis and pericardial effusion (verified by autopsy two weeks following angiocardiographic study). A, frontal teleroentgenogram showing a tremendously enlarged cardiac shadow in an eighteen month old girl. B, frontal angiocardiogram shows a markedly dilated right atrium (RA), right ventricle (RV) and pulmonary artery (PA). Arrows point to the outer border of the huge pericardial effusion.



A B C

FIG. 7. Huge pericardial effusion in a twenty-eight year old man with aneurysmal dilatation of the ascending aorta. A, frontal angiocardiogram showing the large pericardial effusion (arrow). The superior vena cava (SVC) is slightly widened, the right atrium (RA), right ventricle (RV) and pulmonary artery (PA) are normal in size and contour. B, when the left heart is opacified, the left ventricle (LV) is also surrounded by pericardial fluid (arrow). The ascending aorta (AO) is markedly dilated. C, left anterior oblique angiocardiogram also shows the aneurysmally dilated ascending aorta probably due to a *forme fruste* type of Marfan's syndrome complicated by pericardial effusion.



A B

FIG. 8. Noncalcified constrictive pericarditis (verified by operation) in a sixty-five year old man. The cardiac catheterization data (courtesy of Dr. Daniel S. Lukas) showed the classic hemodynamic picture of constrictive pericarditis. A, frontal teleangiocardiogram showing the characteristic dilatation of the superior vena cava and thickening of the pericardium adjacent to the right atrium. B, tracing of A.

by operation, the pericardial fluid being free and nonloculated. Figure 2F is the postoperative film showing the heart to be normal in size and configuration, indicating that the enlarged cardiac silhouette was due to the pericardial effusion.

Angiocardiography in frontal view readily establishes the diagnosis of pericardial effusion by showing the heart surrounded by fluid. In the lateral view the pericardial fluid is anterior (retrosternally) and inferior to the heart chambers. Golden[7] in 1950, in unpublished data, first called attention to the importance of the lateral view in pericardial effusions. He also pointed out that fluid reaccumulated retrosternally because it was the space of least resistance.[8] Recent studies confirm Golden's findings that fluid regularly accumulates retrosternally in pericardial effusions.[2] They also reveal that early in pericardial effusions, or with

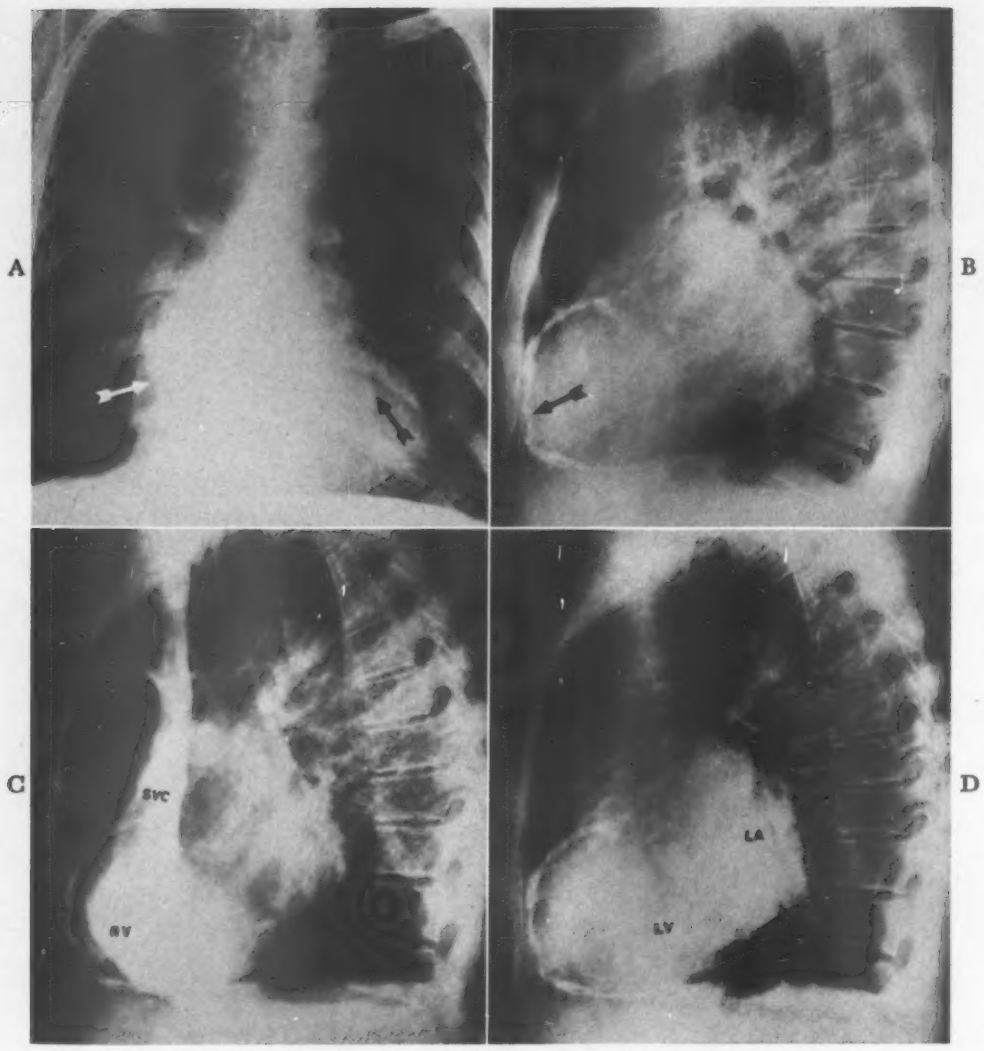
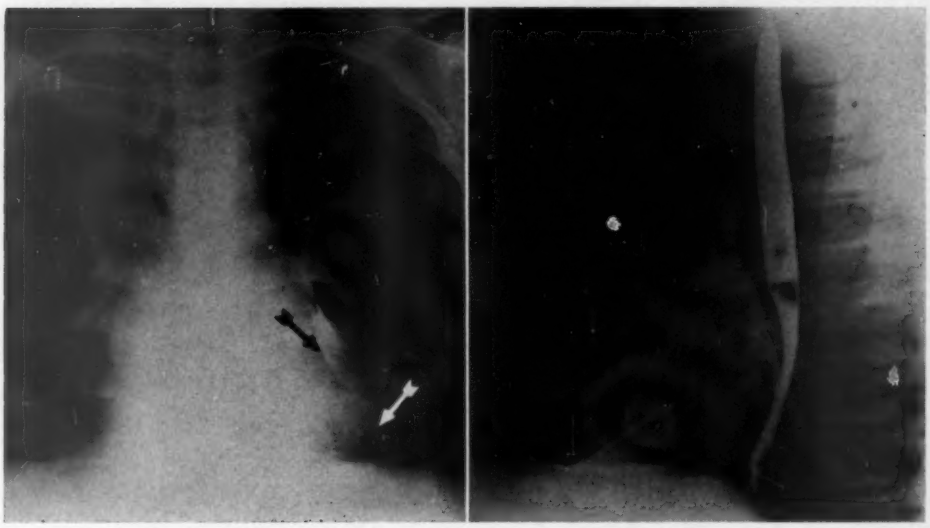


FIG. 9. Constrictive (calcific) pericarditis in a forty-nine year old man with ascites, dependent edema, elevated venous pressure and dyspnea. A, frontal teleroentgenogram showing enlargement of the heart. In this projection the calcified pericardium is seen indistinctly (arrows). B, lateral teleroentgenogram permits recognition of the calcified pericardium (arrow). C, the left anterior oblique angiocardiogram shows the markedly calcified and thickened pericardium well beyond the right ventricular chamber (RV). The superior vena cava (SVC) is widened. D, when the left heart structure is opacified, the left atrium (LA) is enlarged while the left ventricle (LV) and aorta (AO) are normal. The angiocardiographic findings were confirmed at operation (Figure 9C republished with permission of Paul B. Hoeber, Inc.[5])

small effusions, the fluid first accumulates infracardiacally in the most dependent part of the pericardium. It then extends anteriorly and is recognized by alteration (straightening) of the cardiac silhouette especially the left border.

Backward Displacement of Pericardial Pouches: Pericardial effusions apparently never accumulate behind the heart. However, massive pericardial effusions distend the lateral pericardial pouches or recesses and these may extend far backward (Fig. 3). Indeed, inflated water wings (of another era) when held against the chest for swimming assume the same position. This is well illustrated in Figure 3B which shows that the esophagus lies against the posteriorly displaced cardiac chambers, and beyond there is another shadow, the distended pericardial pouch. Pneumopericardial studies (Fig. 3C and D) also show that the pericardial air is anterior. This is because, as Golden[8] believes, the pericardial fluid lies anteriorly where there is no resistance to its accumulation.

The concept that backward displacement of cardiac chambers or the distended pericardial



A B

FIG. 10. Constrictive pericarditis (verified by operation) in a forty-two year old man showing encasement of the heart within a linear calcified pericardium. A, frontal teleroentgenogram showing a plaque of calcium along the left ventricle (arrows). B, the lateral view shows the linear calcified pericardium encasing the cardiac silhouette.

pouches causes compression of the lung helps to understand the mechanism of Ewart's sign.[9] Ewart's sign is an area of dullness, increased fremitus and egophony that occurs in an area of variable size at the inferior angles of the scapula (most often the left) with pericardial effusions. It is apparently nonspecific and has also been described with cardiac enlargement, especially of the left ventricle.[10]

Variations in Pericardial Effusions: Pericardial effusions do not always accumulate in a predictable and uniform manner. Figure 4, for example, shows a greater accumulation of pericardial fluid along the right (Fig. 4B) than the left cardiac border (Fig. 4C). This is probably due to a larger amount of fluid in the right pericardial pouch. In another case (Fig. 5) the infracardiac location of pericardial fluid is striking (Fig. 5B and C). Figure 6 shows a massive pericardial effusion in a child with myocarditis; the dilated cardiac structures contribute significantly to the enlarged cardiac silhouette. Figure 7 is an illustration of pericardial effusion in a patient with a huge ascending aortic aneurysm.

Surgical Treatment: Five patients with massive pericardial effusions treated by incision and drainage of the pericardium were recently reported.[11] Surgical drainage and partial pericardiectomy proved so satisfactory that this procedure is recommended for the treatment of all patients with chronic massive recurrent pericardial effusions. These patients have also shown no recurrence of the effusion for a period varying from two to seven years, an experience duplicated by other reports in the literature.[12,13] Contrary to a recent report,[14] angiocardiography is indicated in those acutely ill and in patients with congestive heart failure and pericarditis because the establishing of a correct diagnosis will lead to life-saving treatment.

Constrictive Pericarditis

The roentgen findings in constrictive pericarditis have recently been reiterated.[15–17] The angiocardiographic aspects of constrictive pericarditis were first reported in 1951.[5] Lately, additional data regarding the value of angiocardiography in the diagnosis of constrictive pericarditis have been published.[19,20] Injection of CO_2 intravenously for visualization of the right atrial wall has also been advocated.[20] Since the contrast agents do such a good job in outlining the cardiac chambers, it is doubtful that CO_2 gas studies for pericarditis (effusive and constrictive) will be used very much.

The older literature described the small quiet heart as being characteristic of constrictive pericarditis. Heinz and Abrams[18] rightly challenge this concept and point out that the cardiac silhouette may appear enlarged and that normal pulsations be apparent. In only 50 per cent of their cases was calcification of the pericardium found, while right ventricular

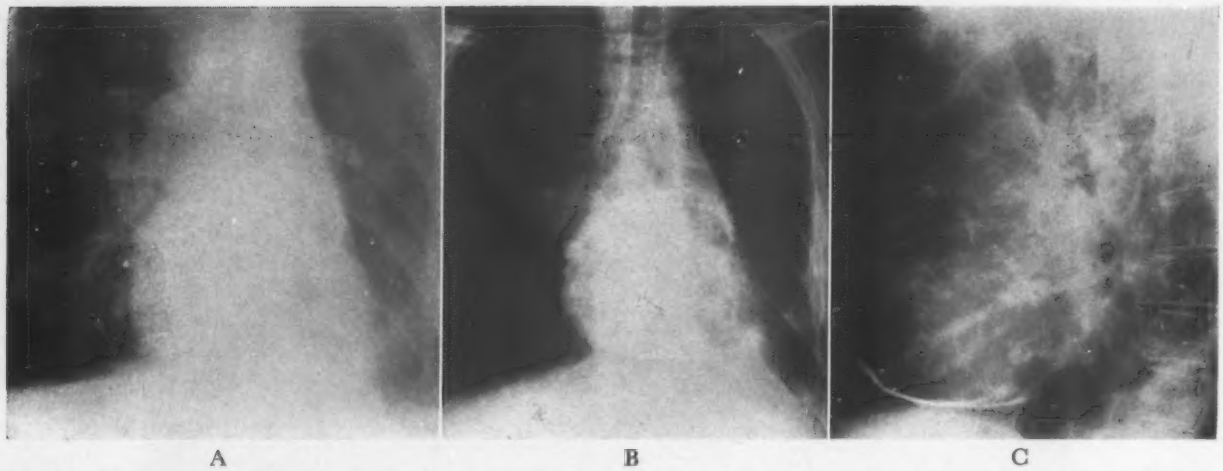


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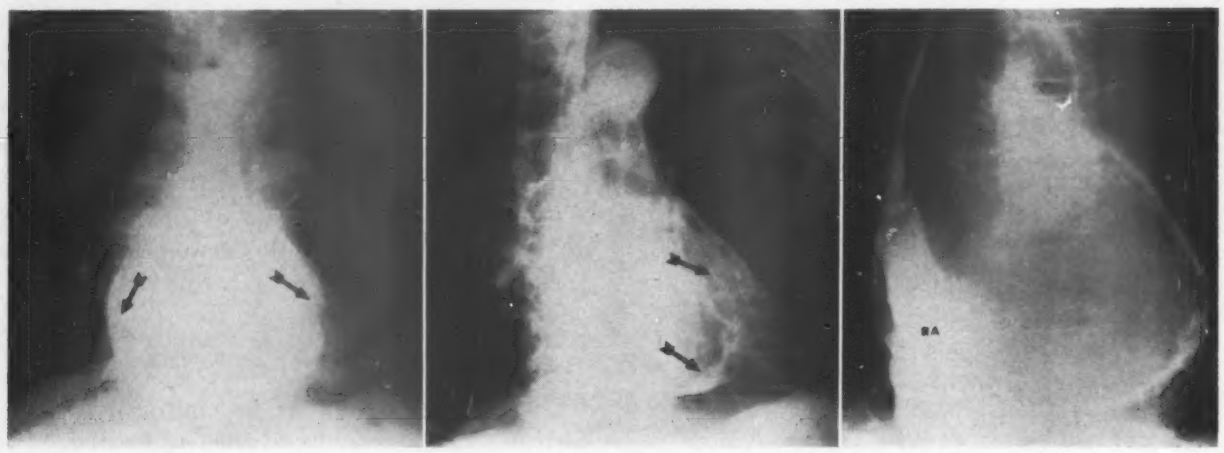
FIG. 11. Chronic constrictive pericarditis (proved by operation) with enlargement of the heart and hemosiderosis of the lungs. A, frontal teleroentgenogram showing cardiac enlargement. The haziness at the left base is due to the pleuritis that followed a previous pericardiectomy. Nodular calcific densities of hemosiderosis are seen at the bases of the lung. In this view the pericardial calcifications are poorly seen. B, overpenetrated frontal roentgenogram clearly shows the thickened calcified pericardium surrounding the heart, especially along the diaphragmatic surfaces. C, lateral view (overpenetrated film) readily reveals the calcified pericardium surrounding the anterior and lower margins of the heart.



A B C

FIG. 12. Calcified (nonconstrictive) pericarditis found incidentally in a fifty-six year old man with syphilitic aortitis. A, conventional frontal roentgenogram shows huge plaques of calcium well within the cardiac silhouette (arrows). B, the right anterior oblique view clearly demonstrates the calcification (arrows) which was not seen in the lateral view. C, frontal angiocardiogram shows the normal sized superior vena cava (SVC) displaced by the syphilitic ascending (as yet unopacified) aorta. The calcifications do not follow the cardiac chamber contours, suggesting that the calcifications are not causing constriction. Findings were later confirmed at autopsy. (Figure 12C republished with permission of Paul B. Hoeber, Inc.[5])

and pulmonary arterial enlargement were common.

Angiocardiographically, increased thickening and rigidity of the right atrial wall, superior vena caval dilatation, slowing of the intrathoracic circulation and often left atrial enlargement can be demonstrated (Figs. 8 and 9).[5,19,20*] It must be emphasized, however, that the angiocardiographic findings in constrictive pericarditis should be used only as a corroborative sign. The definitive diagnosis of constrictive pericarditis rests more upon the clinical and cardiac catheterization data than the roentgen findings.

Calcification of the pericardium, while a valuable sign of constrictive pericarditis (Figs. 10 and 11), is not pathognomonic because extensive pericardial calcification may be present without

* Lyons et al.[30] have described a unique case of vena caval constriction in a patient with constrictive pericarditis. The vena caval constriction was demonstrated preoperatively by angiocardiography and verified at operation.

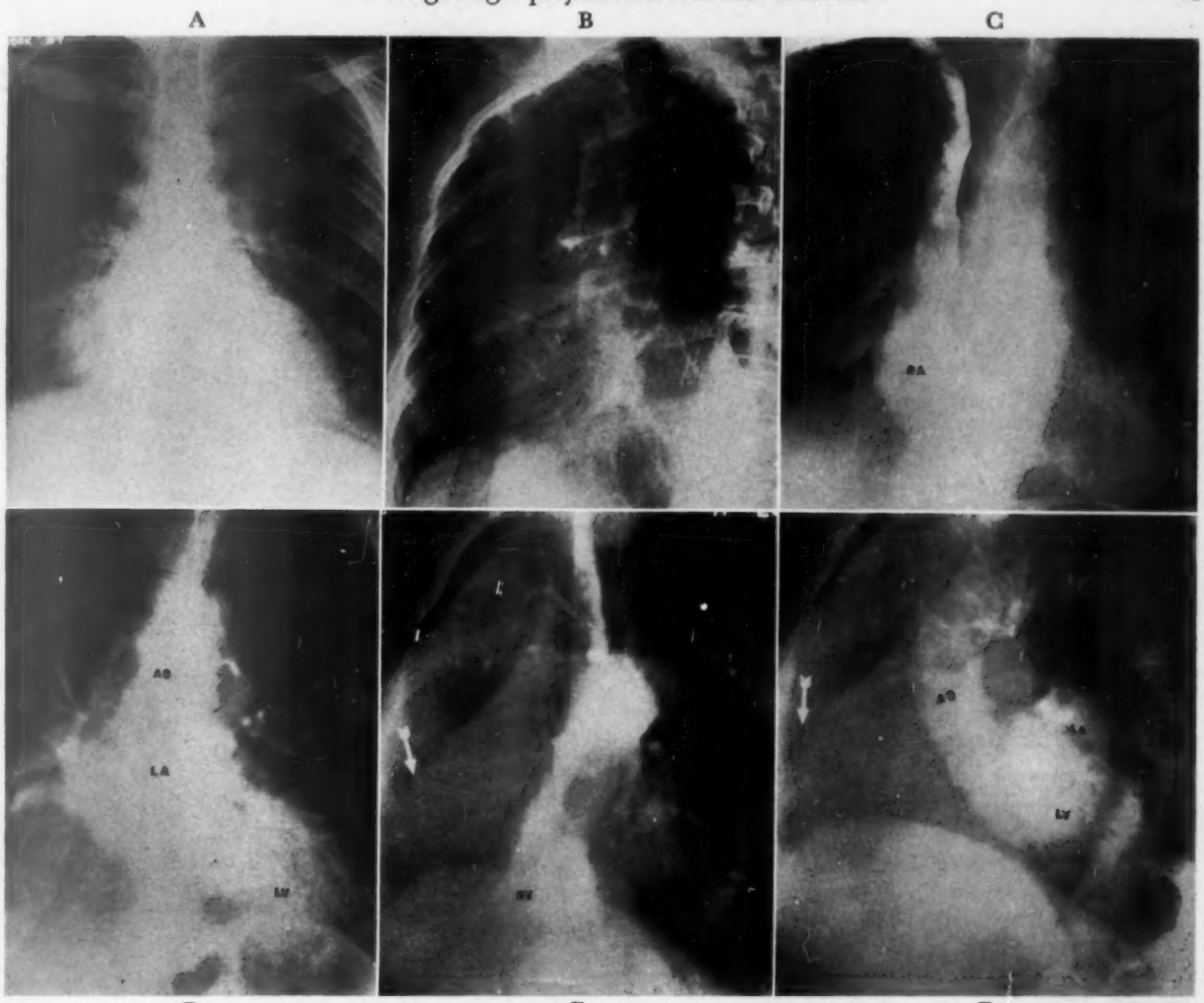


FIG. 13. Pericardial cyst in a fifty-five year old asymptomatic woman (verified by operation). A, frontal teleroentgenogram showing apparent enlargement of the cardiac silhouette. B, the left anterior oblique study suggests enlargement of both the anterior and posterior cardiac chambers. C, the frontal angiocardiogram, however, shows a nonopacified structure adjacent to the right atrium (RA). D, when the left heart is filled, the left ventricle (LV, in diastole) is normal and the wall reaches the left cardiac outline, thereby ruling out pericardial effusion. E, left anterior oblique angiocardiogram shows the large pericardial cyst (arrow) to be adjacent to the right ventricle (RV). F, the left heart structures are normal. The pericardial cyst (arrow) is anterior and behind lower end of sternum.

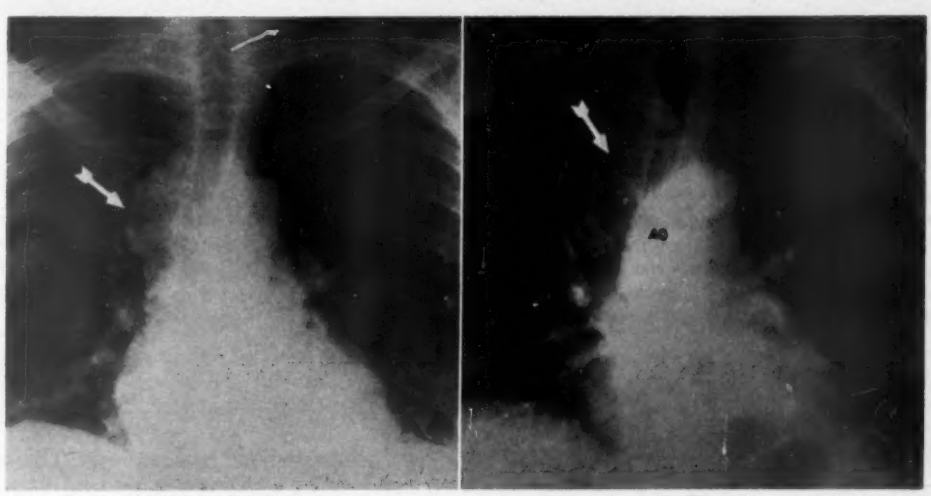


FIG. 14. Pericardial diverticulum in a fifty-six year old asymptomatic woman (verified by operation). A, frontal teleroentgenogram showing a smooth homogeneous mass (arrow) adjacent to the ascending aorta. B, frontal angiocardiogram reveals the normal aorta (AO). The pericardial cyst (arrow) is unopacified and the aorta is intact, thereby ruling out an aortic aneurysm.

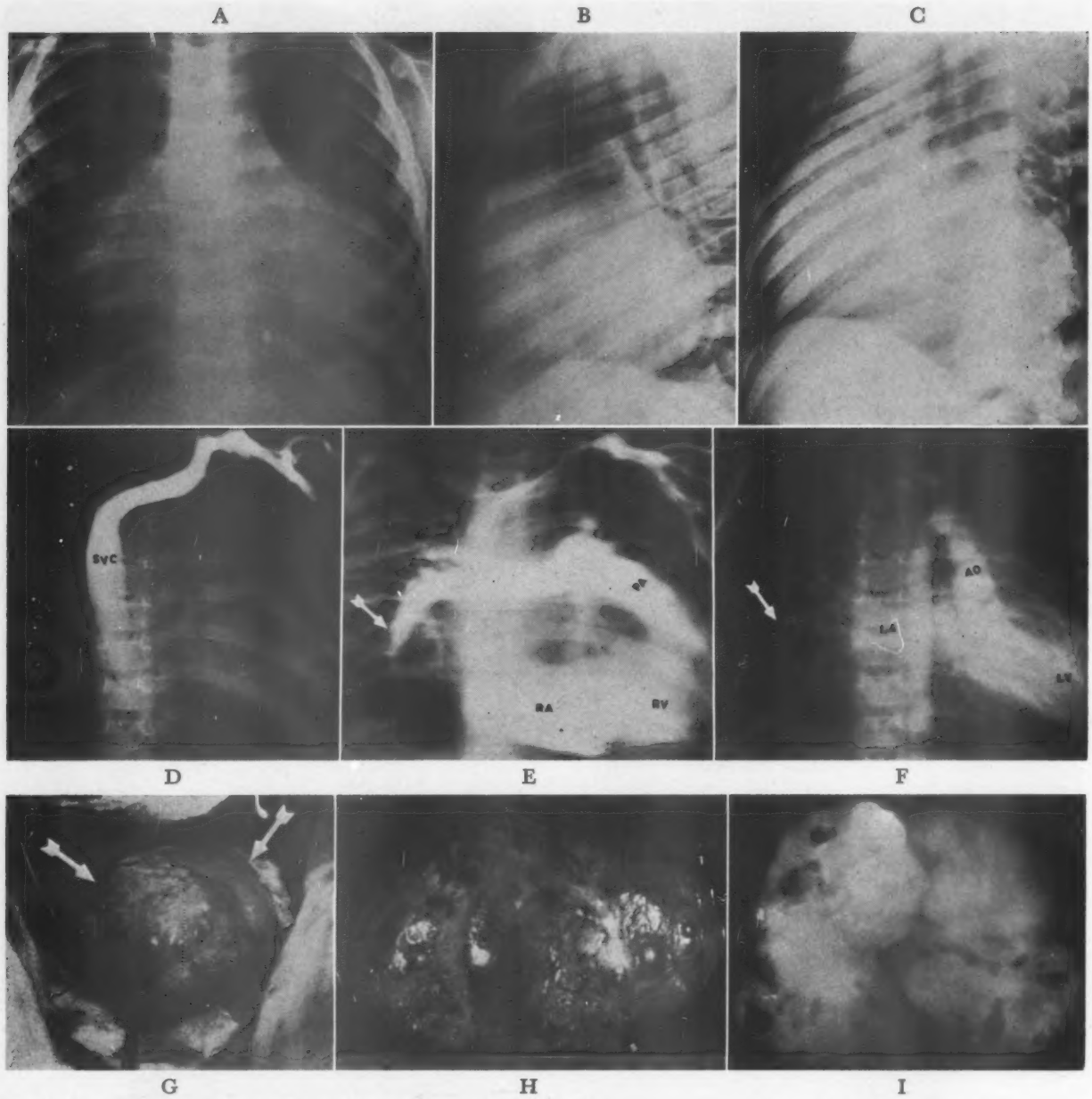


FIG. 15. Intrapericardial bronchogenic cyst in a three year old asymptomatic girl. A, teleroentgenogram shows a huge cardiac silhouette simulating Ebstein's tricuspid deformity or a pericardial effusion. B, the lateral view shows filling of the retrosternal space by the huge cardiac shadow. C, the left anterior oblique projection shows the huge heart extending into the thorax, anteriorly and posteriorly. D, the frontal angiocardiogram shows the superior vena cava (SVC) to be centrally placed. E, later, when the right heart and pulmonary artery are filled there is rotation of the heart into the right anterior oblique position. The superior vena cava and pulmonary artery are displaced by a mass (arrow) which extends well beyond the right atrial border. F, when the left heart structure is opacified, rotation of the heart into the right anterior oblique position by the pericardial tumor (arrow) is evident. G, the pericardial tumor (arrows) at operation appeared larger than the heart. H, photograph of specimen showing the large lobulated tumor. I, roentgenogram of the cut tumor showing the scattered areas of calcifications and cystic nature of the mass.

any cardiac constriction (Fig. 12). Calcification of the pericardium is better seen in the lateral and oblique views (Figs. 9B, C and D; 10B; 11C; and 12C). The calcifications may be linear (Fig. 10B), dense and plaque-like (Figs. 9B, C and D; 10A; 11B and C; 12A, B and C) and often best delineated by overpenetration roentgen technics (Fig. 11B and C).

Pericardial Cysts and Diverticula

Congenital pericardial cysts and diverticula may occur anywhere along the cardiac silhouette

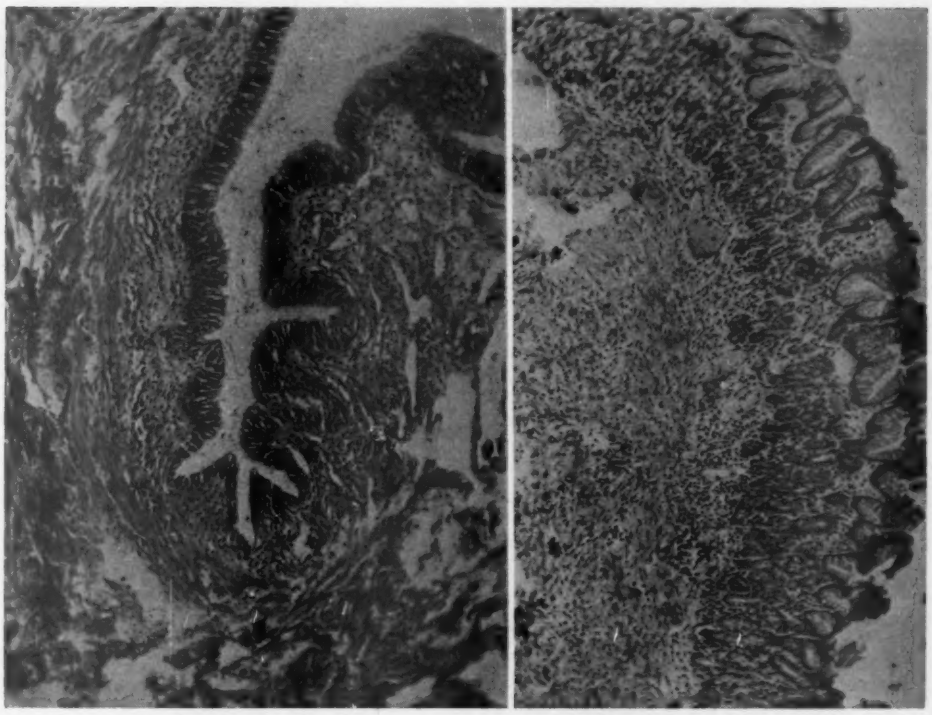
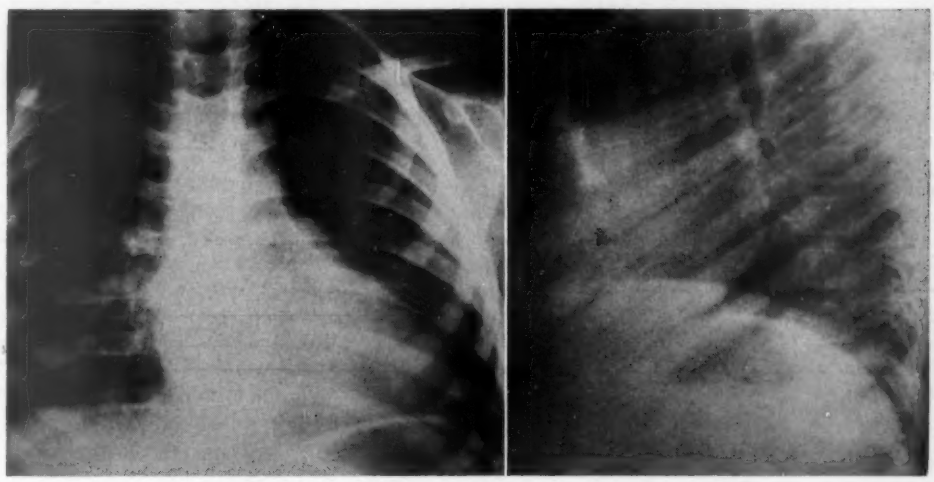


FIG. 15J. Microphotographs (hematoxylin and eosin stain × 60) show bronchial epithelium (right) and gastric mucosa (left).



K L

FIG. 15. K, postoperatively, the frontal roentgenogram showed the heart to be normal. L, similarly, the lateral heart roentgenogram was normal. (Republished with permission of *Am. J. Roentgenol.*[38])

wherever there is reflection of the pericardium. The favorite site appears to be along the right cardiac border (Fig. 13) but they have been reported inferior to the heart and adjacent to the great vessels (Fig. 14). Usually, pericardial cysts and diverticula are well demarcated, rounded or elliptical homogeneous masses occupying the cardiophrenic regions and are frequently indistinguishable from the cardiac shadow. For this reason, angiocardiography is valuable for outlining the cardiac chambers (Fig. 13 D to G). Recently, Fell and associates[21] have recommended air insufflation of suspected diverticula under thoracoscopic control. Roentgen demonstration of a pneumopericardium would then be diagnostic and make exploratory thoracotomy unnecessary. Ellis et al.[22] have also recently described congenital

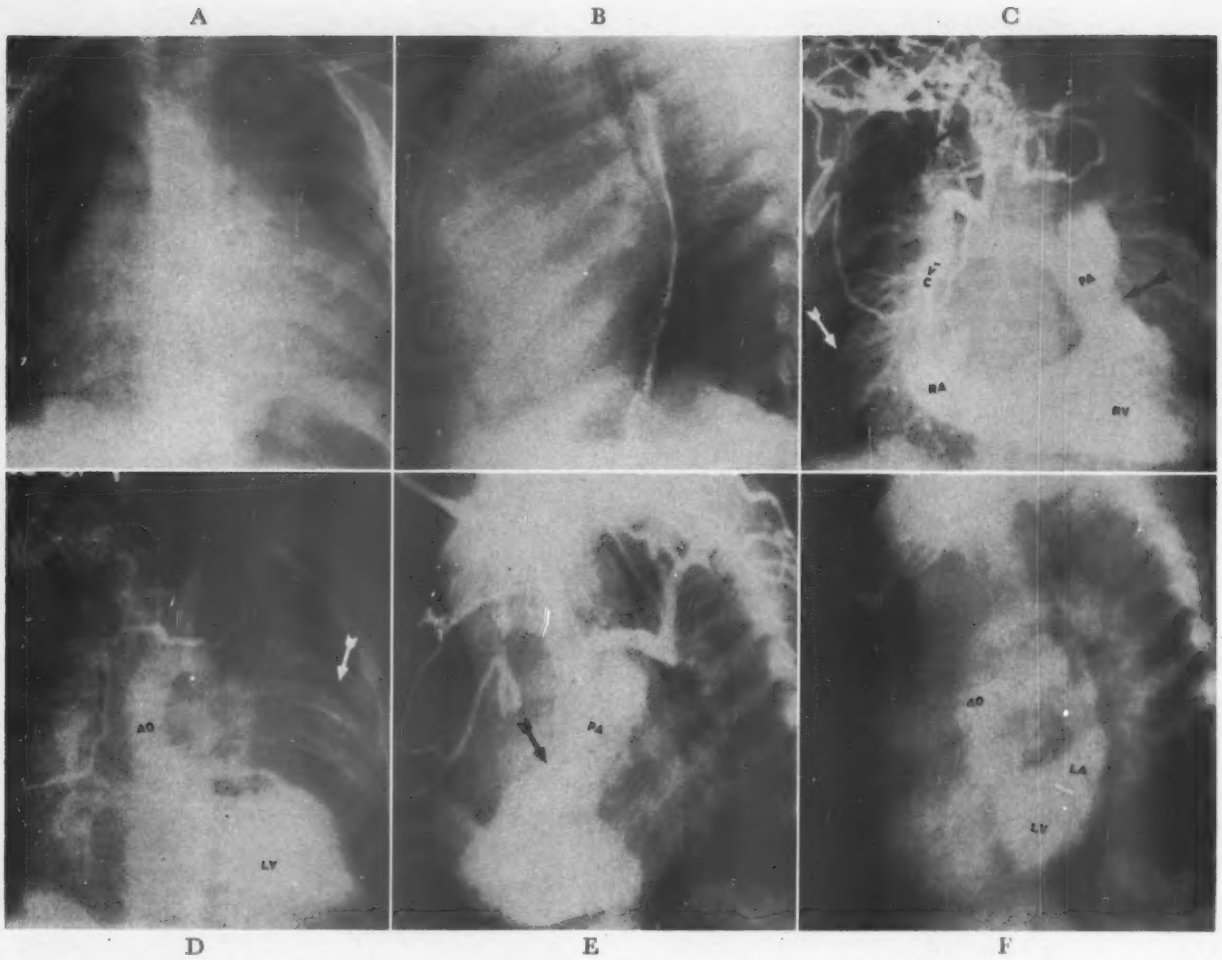


FIG. 16. Teratoid intrapericardial carcinoma in a nine year old girl with complaint of dyspnea (verified by operation and biopsy). A, frontal teleroentgenogram reveals a huge cardiac silhouette. B, the lateral esophagram shows bowing of the sternum and obliteration of the retrosternal space. C, frontal angiocardiogram shows occlusion of the right innominate vein (upper black arrow) with resultant collaterals. The superior vena cava (SVC), while patent, is irregularly narrowed. Note the widely separated superior vena cava and pulmonary artery (PA). There is an unfilled space (white arrow) between the right outer shadow and the opacified right atrium (RA) due to pericardial fluid. The outer margin of the pulmonary conus (lower black arrow) is deformed. D, when the left heart structures are opacified, there is also a large unfilled outer area (arrow) due to pericardial effusion. Wide separation of the ascending and descending aorta suggests that there is tumor at this site. E, the lateral angiocardiogram also discloses deformity of the pulmonary conus (arrow). F, the lateral angiocardiogram also shows unfolding of the aorta (AO) by the tumor. (Republished with permission of *Am. J. Roentgenol.*[36])

deficiencies of the parietal pericardium and advocated left pneumothorax with resultant pneumopericardium for diagnosis.

PRIMARY TUMORS OF THE PERICARDIUM

Primary tumors of the pericardium are rare and usually discovered when a chance x-ray film demonstrates an unusual heart contour.[23] Among the benign pericardial tumors that have been reported are teratomas, fibromas, lipomas, angiomas, leiomyofibromas and cysts. Figure 15 is the roentgen study of a three and one-half year old asymptomatic girl who was found to have a huge cardiac silhouette. Angiocardiography (Fig. 15 D to F) showed unusual rotation of the heart strongly favoring the diagnosis of a pericardial tumor. Such proved to be the case (Fig. 15 G to I). Histologic study showed both bronchial epithelium and gastric mucosa (Fig. 15 J) establishing the diagnosis of a bronchogenic cyst. Dabbs et al.[24,25] have recently reviewed the literature of pericardial bronchogenic cysts and have indicated that angiocardiography plays a significant role in the diagnosis of this condition.

Recently, another patient, aged ten years (Fig. 16), was found to have an intrapericardial teratoid carcinoma with a hemorrhagic peri-

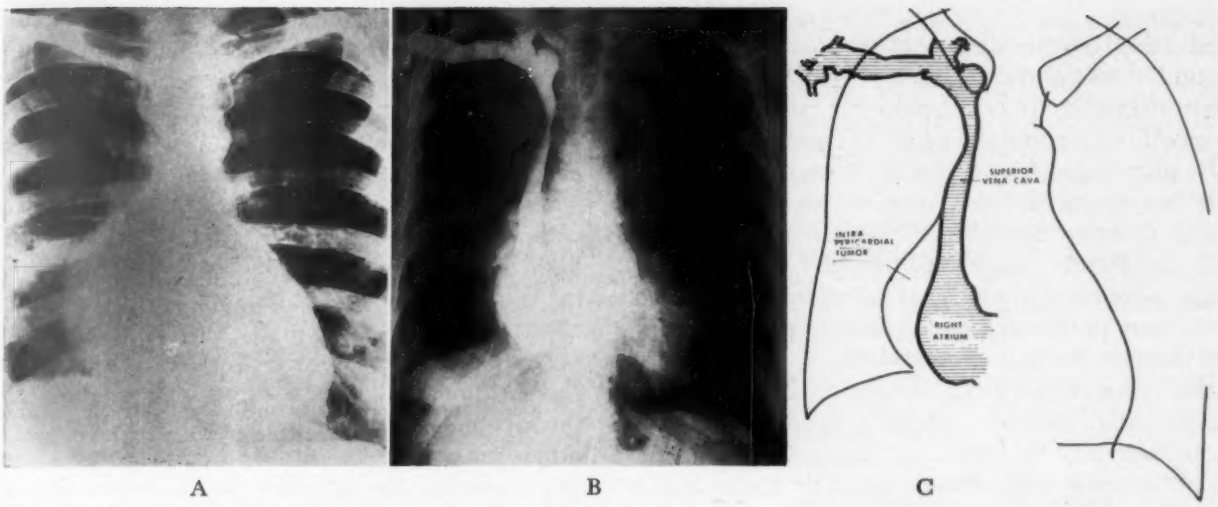


FIG. 17. Pericardial invasion by bronchogenic cancer of the right lung. A, frontal teleroentgenogram showing an unusually prominent right cardiac border. B, frontal angiocardiogram shows the right-sided extracardiac mass. C, tracing of B. (Previously published.[5])

cardial effusion. Angiocardiographic studies disclosed pericardial effusion with invasion of the superior vena cava and rotation of the heart into the right oblique position. Exploratory operation revealed carcinomatous invasion of the superior vena cava which precluded resection of the tumor.

Hemorrhagic pericardial effusions may also occur in patients with benign pericardial tumors. The malignant pericardial tumors (sarcomas) are usually secondary to primary tumors of the heart and are rapidly fatal. A recent review of primary malignant tumors of the heart in infancy was published by Engle and Glenn.[26] Carcinomatous extension into the pericardium from adjacent cancer of the lung may also occur (Fig. 17).

Differential Diagnosis

Ordinarily, mediastinal tumors (dermoids, thymomas, bronchogenic and pericardial cysts) and masses adjacent to the heart (pericardial fat pads and diaphragmatic hernias) are unilateral. Roentgenoscopic study and roentgen positioning are often sufficient to distinguish them from pericardial disease. Occasionally, a huge dermoid, thymoma or lipoma may envelop the heart and defy definite separation. In such instances, angiocardiography by visualizing the cardiovascular structures is very helpful in the differential diagnosis.[36]

As a rule, mediastinal tumors, even large ones, lie to either side of the heart. In such instances, angiocardiography by showing the heart distinct from the mass excludes the diagnosis of pericardial effusion. Two notable exceptions to this have occurred recently. Gerbassi has reported a large horseshoe-shaped pericardial cyst lying anterior to both sides of the heart and occupying both pleural cavities, simulating a pericardial effusion.[27] Another patient (still unreported) showed the characteristic angiocardiographic signs of a pericardial effusion (a normal heart surrounded by a soft tissue mass in frontal view) but at necropsy was found to have massive fatty tissue within the pericardium.

In infancy and childhood the thymus may be huge and defy separation from the heart and pericardium. When cardiac murmurs occur the differential diagnosis of cardiomegaly or of abnormal supracardiac vascular anomalies, such as anomalous pulmonary venous drainage into the left innominate vein, becomes difficult. Visualizing the cardiovascular structures readily reveals the extracardiac thymus or anomalous veins. Recently adrenocortical steroid therapy has been advocated for the differentiation of thymic and cardiac enlargement.[28,29]

Large, dilated and poorly pulsating hearts may sometimes be mistaken for pericardial effusions (Fig. 1). Ebstein's tricuspid valvular deformity is an example of congenital heart disease simulating pericardial effusion. Angiocardiography, however, establishes the diagnosis. Fibroelastosis is another type of congenital heart disease wherein the large heart may simulate a pericardial effusion. Here, too, angiocardiography by revealing the huge distended left ventricle in diastole establishes the

diagnosis. Roentgenographically, chronically advanced rheumatic heart disease with poorly audible murmurs, especially when complicated by tricuspid regurgitation or stenosis, may sometimes be mistaken for pericardial effusions. In such instances careful scrutiny of the mitral or aortic valve areas may reveal calcification and thereby establish the rheumatic valvular involvement. Angiocardiography by revealing the abnormally enlarged chambers will also rule out pericardial involvement. Right atrial myxomas causing tricuspid valve stenosis may also cause right atrial dilatation and simulate pericardial disease. In such instances, angiocardiography by revealing filling defects in the right atrium and ventricle will be diagnostic.

Summary and Conclusions

Roentgenography is essential for diagnosis of pericardial disease. Roentgenoscopy, by revealing motion of the cardiac silhouette, is especially important. The most valuable clue for the diagnosis of pericardial effusion is the recognition of progressive enlargement of the heart shadow in serial roentgen studies. Another valuable aid is the loss of the retrosternal clear space with pericardial effusions. However, enlargement of the outflow tract of the right ventricle in congenital and rheumatic heart disease results in a similar picture. An unusually prominent right or left cardiac contour does not exclude the diagnosis of pericardial effusions because distention of the lateral pericardial pouches occurs often with massive pericardial effusions.

Angiocardiography by delineating the cardiac chambers distinguishes the heart from a surrounding effusion. However, both the right and left heart channels must be visualized to exclude adjacent masses such as mediastinal tumors and pericardial cysts which are usually unilateral. Although the heart is surrounded by fluid in the frontal position in pericardial effusions, in the lateral view the posterior cardiac structures are border forming due to pericardial reflections about the superior and inferior venae cavae and pulmonary veins. Finally, although clinical and electrocardiographic findings should make these instances rare, enlarged hearts due to rheumatic valvular disease (especially tricuspid), and congenital lesions (Ebstein's anomaly, right atrial myxoma and fibroelastosis) may require angiocardiography for differential diagnosis.

Clinical and hemodynamic data are more reliable than roentgenography for the diagnosis of constrictive pericarditis. Angiocardiography will, however, aid in corroborating the diagnosis by establishing widening of the superior vena cava, and thickening and stiffening of the pericardium adjacent to the right atrium. Angiocardiography will also show cardiac chamber enlargement when present but these data by themselves are of no great significance in establishing the diagnosis of pericardial constriction.

Angiocardiography by showing rotation of the cardiovascular structures is important in the diagnosis of intrapericardial tumors. Another important use for angiocardiography in pericardial disease is for the differentiation of adjacent mediastinal tumors. Finally, angiocardiography by revealing enlargement of cardiac chambers and great vessels establishes the diagnosis of various types of heart disease and excludes involvement of the pericardium.

Addendum

Since this paper was submitted for publication, three new papers[31–33] have appeared describing the technic and value of CO_2 gas injected intravenously, chiefly for the diagnosis of pericardial effusion. Despite the enthusiastic reports, it would seem that intravenous angiocardiography, because it allows visualization of the *entire* cardiovascular system, is a superior method for the diagnosis of pericardial disease.

Recently, Maurer and Mendez[34] have advocated intrapericardial injection of gas for diagnosis of pericardial disease. Thoracotomy with incision and exposure of the pericardial contents would appear to be a safer procedure because the accidental transfer of neoplastic or infectious materials into the cardiovascular system will be prevented. Furthermore, the information regarding intrapericardial disease provided by angiocardiography is usually sufficient for diagnosis or else emphasizes the need for surgical exploration of the pericardium.

Finally, Mellins and co-workers[35] have confirmed the angiocardiographic signs of pericardial effusion described above after injecting contrast media into the pericardial sac of animals and making roentgenographic studies of the heart in the thorax.

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Chronic Constrictive Pericarditis*

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ALTHOUGH chronic constrictive pericarditis was first adequately described as early as 1842 by Chevers[1] of Guy's Hospital, the modern attitude toward this uncommon disease probably dates from White's St. Cyres lecture[2] to the staff and guests of the National Heart Hospital in London in 1935. In this historic lecture White described the major features of the disease as we know them today and reported the results of the first twelve patients operated on by Churchill at the Massachusetts General Hospital during the previous five years. The growth of knowledge and experience since then has been considerable, but more in relation to detail than as a result of any great discovery. In this paper an attempt is made to re-emphasize the major features of constrictive pericarditis and its treatment and to describe the more important refinements of knowledge acquired during the past ten to fifteen years.

Definition and Frequency

A mechanical state of constrictive pericarditis may be said to exist when a thickened fibrosed pericardium hampers diastolic filling of the ventricles. No doubt ventricular contraction is also hampered in most cases but this is not usually regarded as an essential feature of the disease.

I have had forty patients with constrictive pericarditis under my personal care. Over the past decade the number of new cases diagnosed each year has varied little, representing between 0.4 and 0.5 per cent of all new cardiovascular material. During this same period constrictive pericarditis proved to be two and a half times less common than the clinically obscure cardiomyopathies and one and a third times more common than primary pulmonary hypertension, the two diseases with which constrictive pericarditis has been occasionally confused. The relative rarity of constrictive pericarditis is emphasized by the fact that White,[3] who has always been particularly interested in this disease, reported a total series of only seventy-eight cases over a period of some twenty-six years, an average of about three cases yearly.

Etiology

Although it is agreed that the majority of cases of constrictive pericarditis are tuberculous in origin, occasional exceptions have been recorded. McKusick,[4] for example, reports a case that developed eighteen months after a gunshot wound of the heart and Mortensen and Warburg[5] report two post-traumatic cases. Nevertheless, I was unable to detect the development of constrictive pericarditis in a single instance in a series of thirty stab, bullet or shrapnel wounds of the heart. Several of these patients were followed long enough for such a development to have taken place, one of them for twenty years. I have not noted constrictive pericarditis occurring after recovery from hemopericardium due to dissecting aneurysm. Three such cases have been followed for several years.

Constriction did not develop after benign pericarditis in fifty cases followed by Carmichael et al.[6] This has been the common experience and none of my cases originally classified as benign has subsequently constricted.

The absence of constriction following rheumatic pericarditis, originally emphasized by White,[2] has been confirmed repeatedly.

Postoperative pericarditis, frequently recurrent, has occurred in about 10 per cent of all direct operations on the heart. It is most common after mitral valvotomy and repair of atrial septal defect because these, perhaps, are the two most common direct cardiac operations at the present time. This type of pericarditis is probably due to a foreign body, particularly an infected suture. Constriction has never developed in

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any of these patients even after two years of repeated attacks. Constriction has never been observed when any of these patients have had a second mitral valvotomy.

Sellors[7] stated that the constriction sometimes followed suppurative pericarditis in a small number of cases. He attributed this to inadequate treatment and remarked that calcification had not been recorded in this group.

Pathology

Subacute Stage: In my series of forty cases, constriction developed in 20 per cent under observation for active tuberculous pericarditis with effusion. Constrictive pericarditis developed in an additional 5 per cent while under observation or treatment for tuberculous pleurisy with effusion. In all but one of these ten patients with active tuberculosis there was an extensive persistent right pleural effusion which was usually aspirated many times; in four instances the effusion spread later to the left side and in one it was bilateral from the start. The pericardial effusion was hemorrhagic in two instances and heavily chylous in one; it was invariably sterile on culture.

These patients with subacute or chronic cases of active tuberculous pericarditis and pleurisy passed imperceptibly into the constrictive state within a period of three months to two years. During the transition stage it was usually impossible to tell whether effusion or constriction was responsible for the high venous pressure. However, it gradually became clear that if signs of cardiac compression did not disappear quickly with antituberculous chemotherapy (streptomycin 1 gm. daily; para-aminosalicylic acid 20 gm. daily; and isoniazid 200 mg. daily), one could be fairly confident that constriction had already occurred. When pericardiectomy was undertaken in such cases, the two layers of the pericardium were sometimes separated by an appreciable quantity of fluid and the constriction was caused entirely by the thickened, heavily fibrosed, contracted visceral pericardium. Calcification, of course, was not a feature of these subacute cases.

Chronic Stage: In 75 per cent (thirty cases) of this series constrictive pericarditis presented in an already fixed and chronic state, years after the initial inflammation that caused it. Biopsy of the pericardium confirmed the inactivity, but in one instance tubercle bacilli were revealed on culture. In the majority of this group the visceral and parietal pericardium were fused into a thick, fibrous, unyielding mat, varying between 1 mm. and 7.5 mm. in depth. Such a mat was often far from uniform, some areas escaping the brunt of the attack and others being heavily banded, particularly in the atrioventricular groove. The greater part of the surface of both ventricles, however, was involved in all cases and localized atrial or caval constriction was never seen. While it is agreed that extensive calcification is present in only half of all cases of constrictive pericarditis, it is pointed out that if subacute active or recently active cases are excluded, heavy calcification is noted in 70 per cent of the remainder. This was the figure in this series and it cannot be very different in others; published figures for the total incidence of calcification are remarkably uniform and all series must contain an appreciable number of still active cases in which calcification is not present. Indeed, the frequency of this condition in any given series gives a good indication at once of the nature of the material.

Extension of fibrosis into the superficial layers of the myocardium occurred in some cases but its degree was difficult to assess.

The most obvious result of pericardiectomy was improved diastolic filling and stroke output.

Clinical Features

Age and Sex: The average age of the forty patients in this series was forty-two years, and the age distribution was fairly uniform between twenty and seventy years. There was a slightly increased concentration during the fifth decade. Tuberculous activity was not related to age in adults, but the only two patients under the age of twenty years (thirteen and eighteen years) demonstrated tuberculous activity. The male to female sex ratio was 2:7. This age and sex distribution is similar to that given in most clinical articles on constrictive pericarditis.

Onset Following Tuberculous Pericarditis: One-quarter of the patients had an acute, subacute or insidious onset of their illness with what proved to be active tuberculous pericarditis although it was not recognized as such at the time. None received early treatment with antibiotics. Conversely, 80 to 90 per cent of patients with acute tuberculous pericarditis who are treated properly within a few weeks of the onset of disease do not develop constriction.[8] I have had the opportunity of treating only eight patients with active tuberculous pericardi-

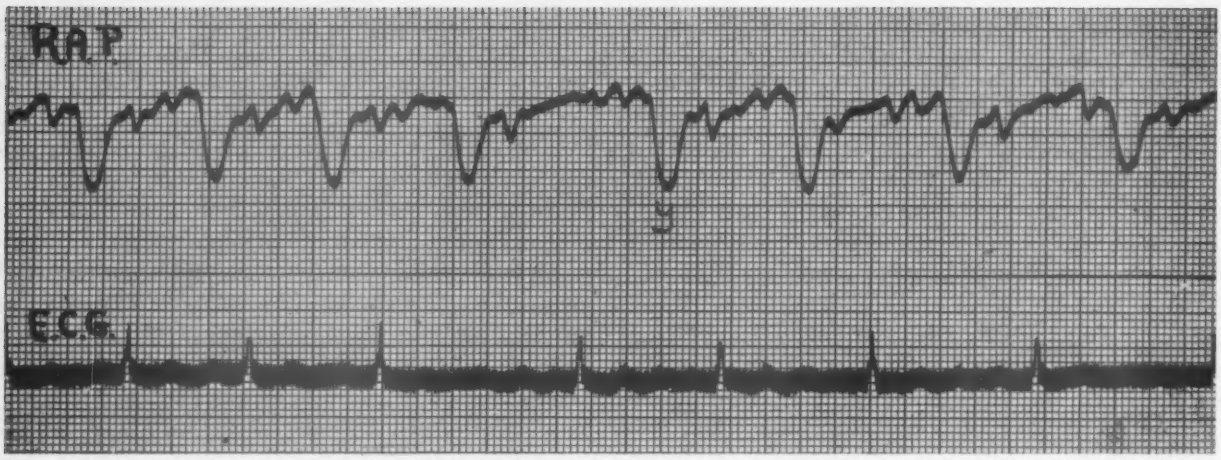

FIG. 1. Steep *y* descent and deep *y* trough in right atrial (and jugular) pressure pulse in a patient with constrictive pericarditis with atrial fibrillation.

tis within two months of the onset and all recovered without constriction after receiving streptomycin, 1 gm. daily, with or without para-aminosalicylic acid, 15 to 20 gm. daily or isoniazid, 200 to 300 mg. daily for a minimum period of three months. Three of these patients have now been followed for a period of ten years and have remained well and free from constriction.

SYMPTOMS

Ascites and Edema: In chronic cases the first symptom is usually swelling of the abdomen from enlargement of the liver, with or without ascites. Although it is generally stated that ascites is disproportionate to edema,[9] in the present series ascites did not occur alone in any instance but was combined with edema in 55 per cent, edema occurred alone in 13 per cent and neither was present in the remainder of patients. The early abdominal swelling and discomfort of chronic constrictive pericarditis is due to enlargement of the liver which is proportional to the height of the venous pressure. At this stage the patient is otherwise relatively well. With comparable rises of venous pressure patients with cardiomyopathy complain much more of fatigue and breathlessness and patients with pure right ventricular failure or with tricuspid stenosis, in whom breathlessness may not be pronounced, still complain of fatigue. The relative well-being of patients with constrictive pericarditis may be attributed to the fact that the cardiac output is fairly well maintained at this stage. By the time portal hypertension is sufficient to encourage ascites, edema is almost invariably present.

In the hope of clarifying some of the confusion that has surrounded this subject it may be helpful to make the following observations: (1) Hepatic enlargement and ascites are no more frequent or severe in constrictive pericarditis than in disease of the tricuspid valve, pure right ventricular failure or heart failure from cardiomyopathy with a comparable sustained rise of venous pressure (mean). (2) Cardiac edema depends more on reduction of cardiac output and renal blood flow than upon height of the venous pressure.[10,11] (3) As will be noted later in this paper, cardiac output is usually better maintained in constrictive pericarditis than in heart failure with a comparable rise of venous pressure. (4) Ascites may occur without edema in patients with active tuberculosis when it is more likely to be caused by tuberculous peritonitis.[7]

Increasing experience is adding to the frequency with which active tuberculous pericarditis is recognized. In a recent report of sixty-two cases of constrictive pericarditis by Gimlette,[12] for example, the constrictive process developed within one year of the acute attack of pericarditis in twenty-eight patients. Excluding half a dozen cases due to nontuberculous causes, this means that 41 per cent of Gimlette's patients with probable tuberculosis were still active when they entered the constrictive phase.

Breathlessness: Although some degree of breathlessness develops sooner or later in nearly all cases of constrictive pericarditis severe enough to warrant pericardiectomy, and did so in the present series, most authors have stressed its relative insignificance. The impression has grown that constrictive pericarditis behaves like right ventricular failure, the obstruction to cardiac filling damming up the blood in the

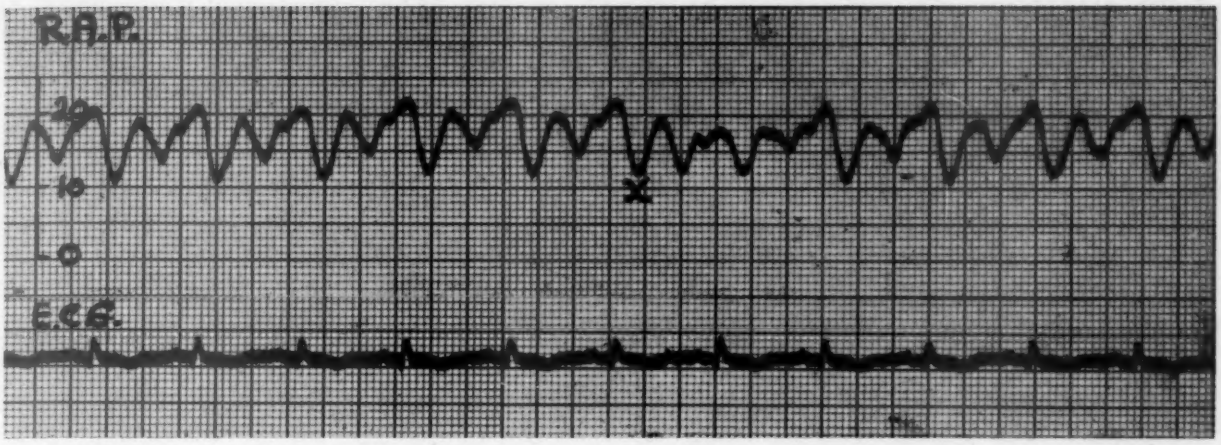

FIG. 2. Sharp *x* descent in right atrial (and jugular) pressure pulse in a patient with constrictive pericarditis with normal sinus rhythm.

systemic venous system but not in the lungs. This myth has been exploded by cardiac catheterization which has consistently demonstrated that the pulmonary venous pressure is as high or higher than the systemic. The suggestion[9] that patients with orthopnea have predominant left-sided constriction is not borne out by the facts. In my series orthopnea occurred in 46 per cent of the patients who required surgical treatment and Gimlette[12] claimed that orthopnea occurred in 90 per cent of the patients in his series. Even in these cases, however, left and right atrial pressures remained obstinately similar. It is probably true that the pulmonary venous pressure rarely rises high enough to cause interstitial edema of the lung, that paroxysmal cardiac dyspnea is rare and that orthopnea is voluntary rather than imperative.

PHYSICAL SIGNS

When patients with chronic constrictive pericarditis first seek medical advice, they usually appear healthy. It is only the jugular venous pulse and distended abdomen which at first glance reveal their plight. Unless the patient has ignored his symptoms for a very long time, obvious breathlessness at rest, peripheral cyanosis and general distress usually mean activity with or without associated pleural effusion. Other evidence of activity should always be diligently looked for.

Arterial Pulse and Blood Pressure: The pulse is usually said to be rather small and sometimes paradoxical, and the systolic blood pressure and pulse pressure both rather low. While these tendencies cannot be denied, they must not mislead us in differential diagnosis. In the present series (omitting three exceptional cases with blood pressures close to 165/105 mm. Hg) the blood pressure averaged 120/78 mm. Hg, giving an average pulse pressure of 42 mm. Hg. The pulse pressure ranged between 20 mm. Hg and 35 mm. Hg in 40 per cent of the cases. The pulse was convincingly paradoxical in five of the ten cases of active pericarditis, but in only 15 per cent of the inactive majority. It should be emphasized that the volume of the pulse in chronic, inactive constrictive pericarditis is apt to be maintained better than in cases of myopathic heart failure with a similar degree of venous hypertension, because the cardiac output is usually higher in the former. For the same reason, peripheral vasoconstriction may be more intense in myopathic heart failure in which blood pressures about 130/100 mm. Hg are not uncommon.

Venous Pulse: The jugular venous pressure is necessarily raised in constrictive pericarditis. Neither a heavily fibrosed nor calcified pericardium can properly be called constrictive unless diastolic filling of the ventricles is hampered. The most characteristic feature of the venous pulse, which has been known for over a century, is the diastolic collapse of Friedreich,[13] i.e., a sharp *y* descent and deep *y* trough (Fig. 1). This type of venous pulse represents a high filling pressure, sudden release of pressure due to rapid tricuspid inflow, followed by a sharp rise of pressure when further expansion of the ventricles is prevented by the rigid pericardium. A similar form of venous pulse may be seen in cases of heart failure in which a high venous pressure is associated with an overloaded right ventricle which resists late diastolic filling. Its chief clinical importance is to deny tricuspid stenosis.

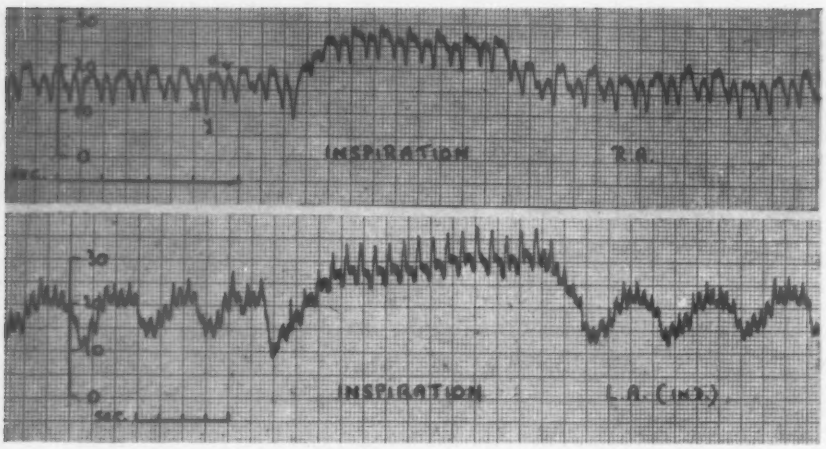

FIG. 3. Effect of inspiration on the left (below) and right (above) atrial pressures in a patient with constrictive pericarditis.

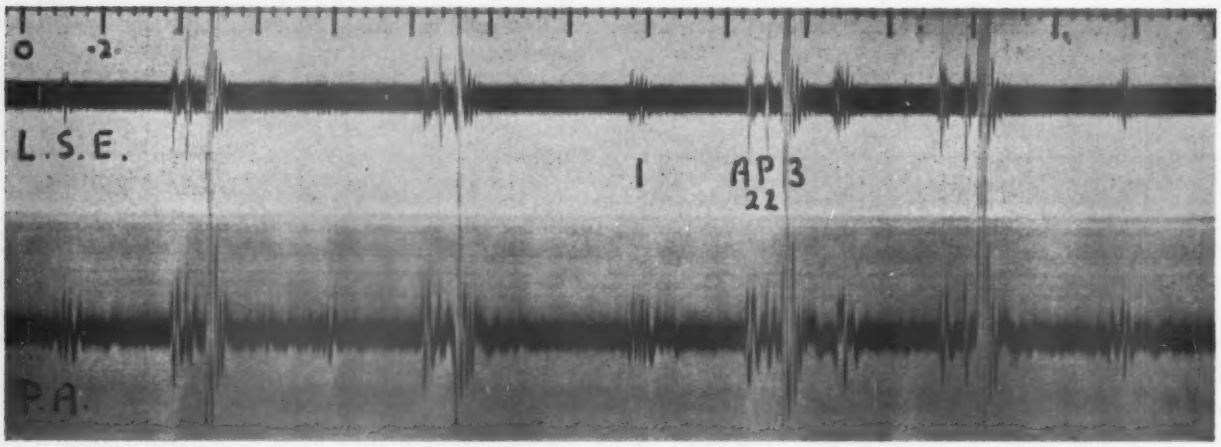

FIG. 4. Loud early third heart sound 0.10 second after A_2 in a patient with constrictive pericarditis.

Gibson[14] has recently drawn attention to an equally sharp or even sharper and deeper *x* descent in some cases of constrictive pericarditis (Fig. 2). This is attributed to exceptional descent of the base during systole when the lateral walls of the ventricles have difficulty in moving inward. This sharp *x* descent may prove helpful in differential diagnosis for it does not seem to be a feature of heart failure or of tricuspid stenosis.

Paradoxical Pulse: Both systemic and pulmonary venous pressures rise conspicuously on inspiration when descent of the diaphragm further tenses the pericardium. The rise in systemic venous pressure can be inspected in the neck. Increased obstruction to left ventricular inflow, which causes the rise of pulmonary venous pressure, may be reflected in a diminished pulse volume (paradoxical pulse). The double effect of inspiration on the pressures in the two venous systems has been demonstrated almost routinely during cardiac catheterization (Fig. 3). In differential diagnosis, however, an inspiratory rise in jugular venous pressure (Kussmaul's sign) cannot be accepted as evidence of constrictive pericarditis, for it is frequently noted in cases of heart failure.

Atrial Arrhythmias: Atrial fibrillation (35 per cent) or atrial flutter (10 per cent) occurred in 45 per cent of the patients in the series. This compares closely with the 44 per cent figure recorded by Dalton, Pearson and White.[3] Atrial arrhythmias were related more to the duration of the disease than to the age of the patient. Thus, average age of those with atrial fibrillation or flutter was forty-five years and the average age of those with normal rhythm was forty-one years. On the other hand, only one of the ten patients with active pericarditis had an atrial arrhythmia in contrast with 70 per cent of the inactive cases in which the patients had had constrictive pericarditis for a much longer time. The difference between the two sets of figures is so remarkable that in differential

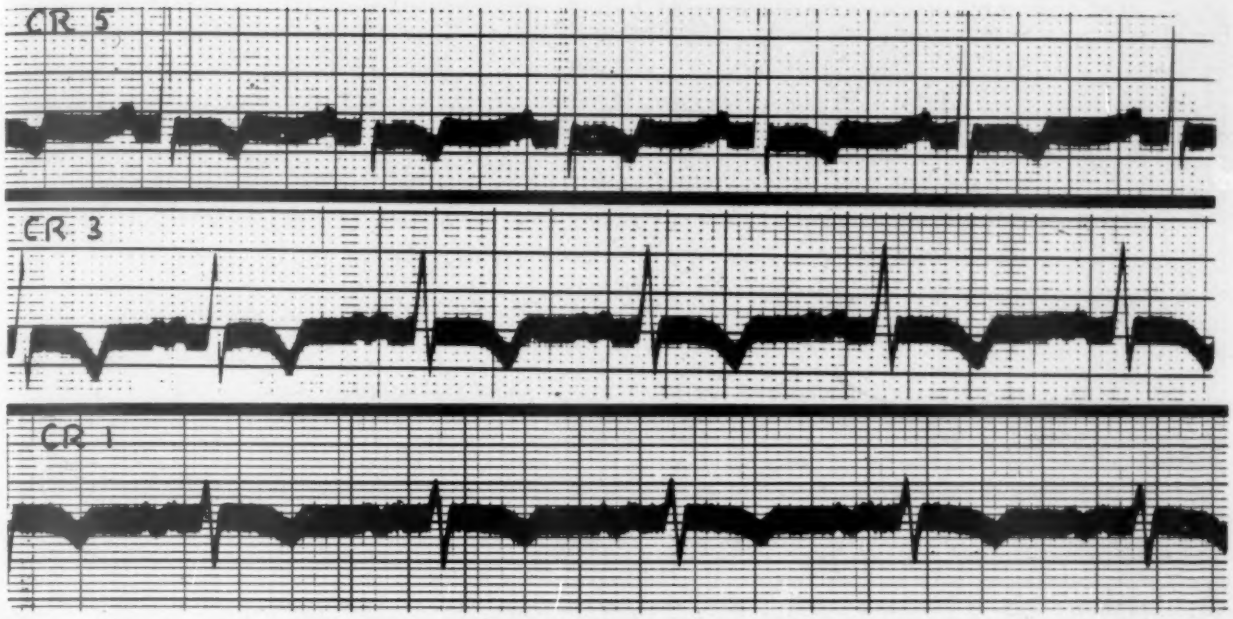

FIG. 5. Electrocardiogram (precordial leads) showing P mitrale in constrictive pericarditis.

diagnosis not only does atrial fibrillation suggest inactive disease of long duration but also normal rhythm actually favors activity. The association of a sharp *x* descent and atrial fibrillation gives rise to a rare type of venous pulse, for it is very unusual to observe two obvious troughs per cardiac cycle in cases of atrial fibrillation. This at once may suggest the diagnosis of constrictive pericarditis.

Typical Cardiac Signs: The lack of a properly defined cardiac impulse has been noted by most observers. In the present series it was absent in 90 per cent of the patients and this is highly characteristic of the disease.

On auscultation the most important finding is the loud early third heart sound (Fig. 4) described by Evans and Jackson.[15] This is the palpable diastolic shock of earlier writers. Phonocardiography places it between 0.09 and 0.12 second after closure of the aortic valve, which is appreciably earlier than the normal third heart sound (about 0.15 second after A_2). In timing and character this loud, sharp, early third sound may resemble a late opening snap. The sound is attributed to the early limit to left ventricular filling imposed by the rigid, constricted pericardium.

Marked enlargement of the liver and often of the spleen, with or without ascites and edema, complete the physical signs.

ELECTROCARDIOGRAM

The electrocardiogram revealed the classic features of constrictive pericarditis in 90 per cent of the present series but was within normal limits in the remainder. The essential abnormality is widespread flattening or simple inversion of the T wave without deformity of the

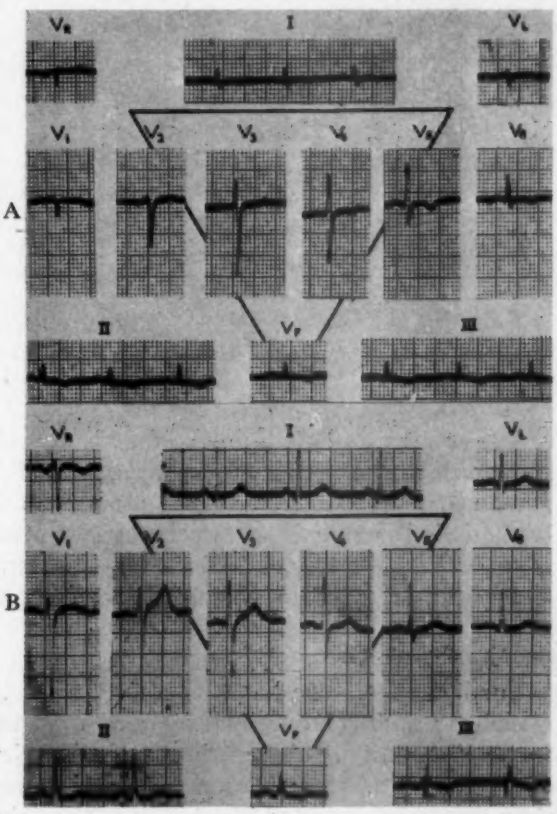

FIG. 6. A, electrocardiogram obtained before pericardiectomy (April 22, 1953). B, electrocardiogram obtained after pericardiectomy (October 8, 1956), demonstrating resolution to normal.

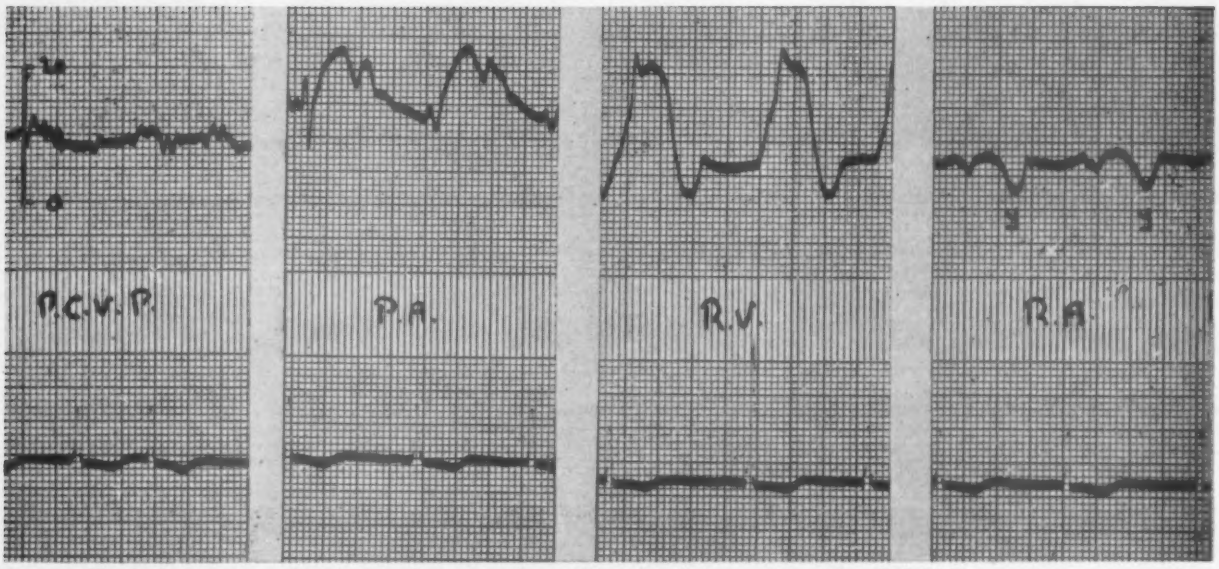

FIG. 7. Typical pressure pulse tracings from a patient with constrictive pericarditis. P.C.V.P. = pulmonary capillary venous pressure; P.A. = pulmonary artery; R.V. = right ventricle; R.A. = right atrium.

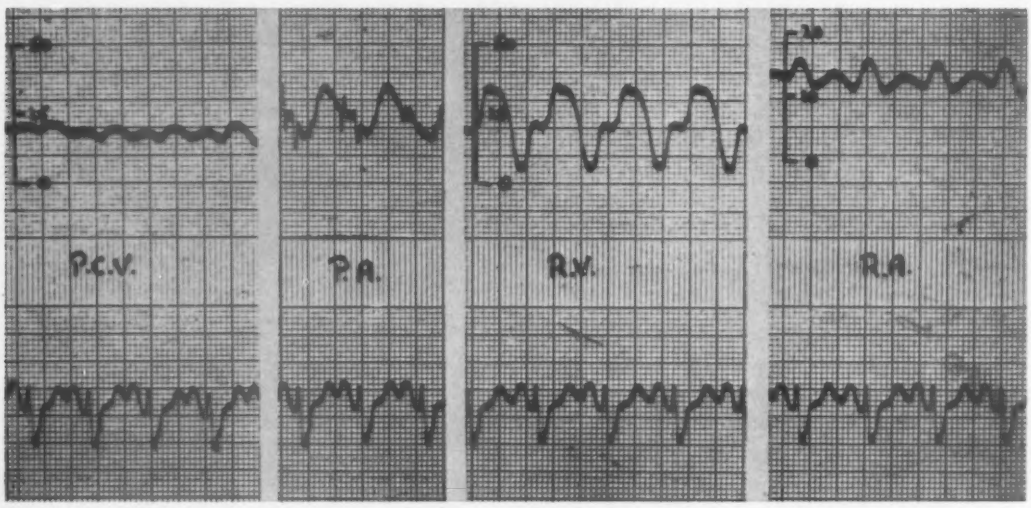

FIG. 8. Sharp early diastolic dip and rebound in the right ventricular pressure pulse (R.V.) from a patient with cardiomyopathy (subsequently proved at necropsy).

QRS complex, although low voltage is the rule. In addition, the P wave may be deformed, a *P mitrale* being particularly common (Fig. 5). While it is the rule for these changes to persist after pericardiectomy, occasionally the electrocardiogram returns to normal limits (Fig. 6).

X-RAY APPEARANCES

Further experience has added nothing to the radiologic findings described by earlier workers such as Freedman.[16] These findings include lack of cardiac enlargement, or less enlargement than would be expected in relation to the height of the venous pressure, pericardial calcification in about half the cases, triangular shape with some loss of definition (particularly of normal angles) and relatively poor pulsation fluoroscopically. Calcification is not noted in patients with active pericarditis. If these patients are excluded from any given series, calcification is likely to be revealed in over two-thirds of the majority of patients with inactive pericarditis (70 per cent of the thirty such patients in the present series).

When the heart shadow is considerably enlarged, residual pericardial effusion may be assumed present. This indicates activity. More than slight enlargement was not detected radiologically in a single patient with inactive pericarditis in the present series.

In differential diagnosis, lack of cardiac pulsation does not help to distinguish constric-

TABLE I

Hemodynamic Findings in Constrictive Pericarditis and Cardiomyopathy

Case No.	Age	Chief Wave in JVP*	Mean RAP† (mm. Hg)	Mean LAP‡ (mm. Hg)	LA-RA Pressure Difference (mm. Hg)	PAP§ (mm.Hg)	PA-LA Gradient Pressure Difference (mm. Hg)	Pulmonary Vascular Resistance Units	A-V‖ Oxygen Difference ml./L.	Cardiac Output (L./minute)	Rhythm
A. Eight Patients with Active Constrictive Pericarditis											
15	23	x	12	13	1	23/15	5	1	48	5.2	Normal
23	18	x	16	17	1	30/20	8	1.8	56	4.3	Normal
25	58	x	8	10	2	25/15	7	1.7	51	4.1	Normal
26	30	x	17	20	3	35/20	5	1.4	58	3.5	Normal
29	68	x	12	9	−3	45/17	16	3.4	44	4.7	Normal
34	13	x	15	15	0	33/19	9	2.2	46	4.0	Normal
38	32	y	10	16	6	30/10	4	1.1	72	3.8	Atrial fibrillation
41	38	y	10	13	3	30/15	9	1.4	35	6.3	Normal
Average	35	x	12.5	14.1	1.6	31/16	8	1.75	51	4.5	Normal
B. Thirteen Patients with Inactive Constrictive Pericarditis											
9	58	y	10	10	0	25/16	7	...	52	...	Atrial fibrillation
10	63	xy	4	10	6	27/11	8	1.8	48	4.5	Atrial fibrillation
11	28	y	13	22	9	32/22	5	0.8	44	6.0	Normal
13	47	y	8	11	3	22/13	5	0.8	37	6.2	Atrial fibrillation
14	49	y	16	17	1	37/21	10	3.1	53	3.2	Atrial fibrillation
17	63	y	4	5	1	22/12	12	2.2	43	5.4	Atrial fibrillation
18	67	xy	3	3	0	16/7	7	2	58	3.5	Normal
19	41	x	11	16	5	20/10	5	1.2	65	4.0	Normal
21	25	y	[2]	...	...	24/9	...	...	70	3.2	Atrial fibrillation
28	60	x	5	7	2	33/12	11	2.7	51	4.0	Atrial fibrillation
30	28	y	14	20	6	35/25	10	1.4	43	6.9	Normal
35	41	xy	17	14	−3	28/18	8	1.6	71	5.0	Atrial fibrillation
37	55	y	6	11	5	30/15	10	1.4	34	6.9	Atrial fibrillation
Average	48	y	9.3	12.2	2.9	27/15	8.2	1.7	51	4.8	Atrial fibrillation
C. Ten Patients with Cardiomyopathy Which Clinically Resembled Constrictive Pericarditis											
3	42	...	2	...	...	26/14	...	Approx. 2	83	3.3	Normal
4	13	ay	12	20	8	42/24	10	Approx. 3	69	...	Normal
23	27	y	11	14	3	29/14	5	Low	59	...	Normal
25	45	av	6	26	20	55/37	14	4.2	102	3.4	Normal
48	37	v	10	16	6	62/40	30	10	90	3	Atrial fibrillation
51	50	y	2	20	18	55/30	15	2.9	50	5.2	Atrial fibrillation
54	51	a	12	15	3	62/30	25	11.4	95	2.2	Normal
56	43	a	3	24	21	52/30	16	4	73	4	Normal
64	23	a	2	16	14	40/20	9	2.6	67	3.5	Normal
85	32	y	11	24	13	55/27	16	4.6	69	3.5	Normal
Average	36	a or y	7.1	19.4	12.3	48/27	15.5	...	75	3.5	Normal

* JVP = Jugular venous pulse; † RAP = Right atrial pressure; ‡ LAP = Left atrial pressure; § PAP = Pulmonary artery pressure; ‖ A-V = Arteriovenous.

tive pericarditis from cardiomyopathic failure without mitral or tricuspid incompetence.

HEMODYNAMICS

Characteristic findings elicited by means of cardiac catheterization (Fig. 7) include elevated right and left atrial pressures, a sharp *y* descent and deep *y* trough in the majority of right and left atrial pressure pulse tracings, a conspicuous early diastolic dip synchronous with this *y* trough in right and left ventricular pressure pulses, elevated end-diastolic pressures in both ventricles equivalent to their respective end-diastolic atrial pressures, and a stroke output that varies little in response to changes of venous filling pressures (Tables IA and B). Typical tracings have been published by many authors.[17–20] The Valsalva maneuver usually gives rise to a more or less square wave type of response.

Although all these features are characteristic and may be recorded routinely in cases of chronic constrictive pericarditis, they are not diagnostic and all of them may be observed in patients with heart failure with a comparable rise of venous pressure (Fig. 8). Since the differential

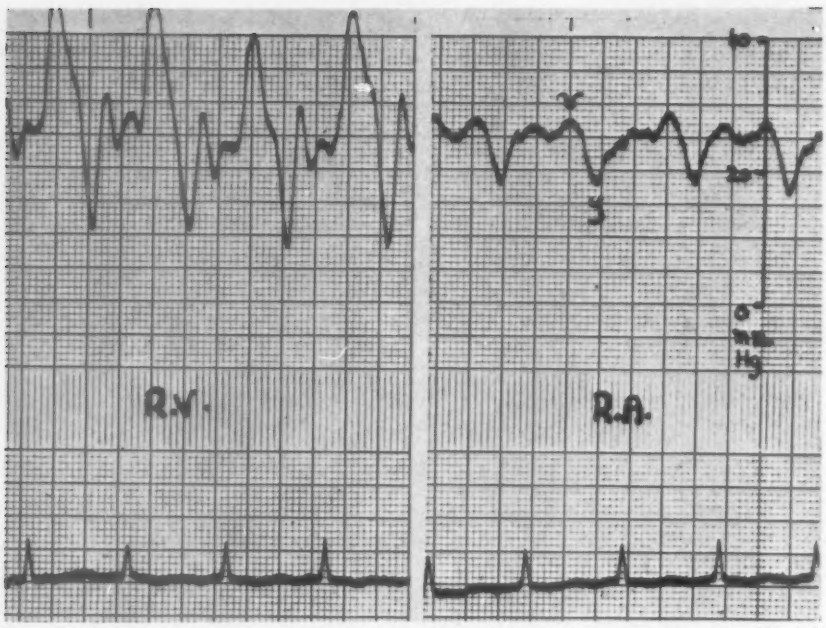

FIG. 9. Steep *y* descent and deep *y* trough in right atrial pressure pulse (R.A.) from a patient with cardiomyopathy (subsequently proved at necropsy).

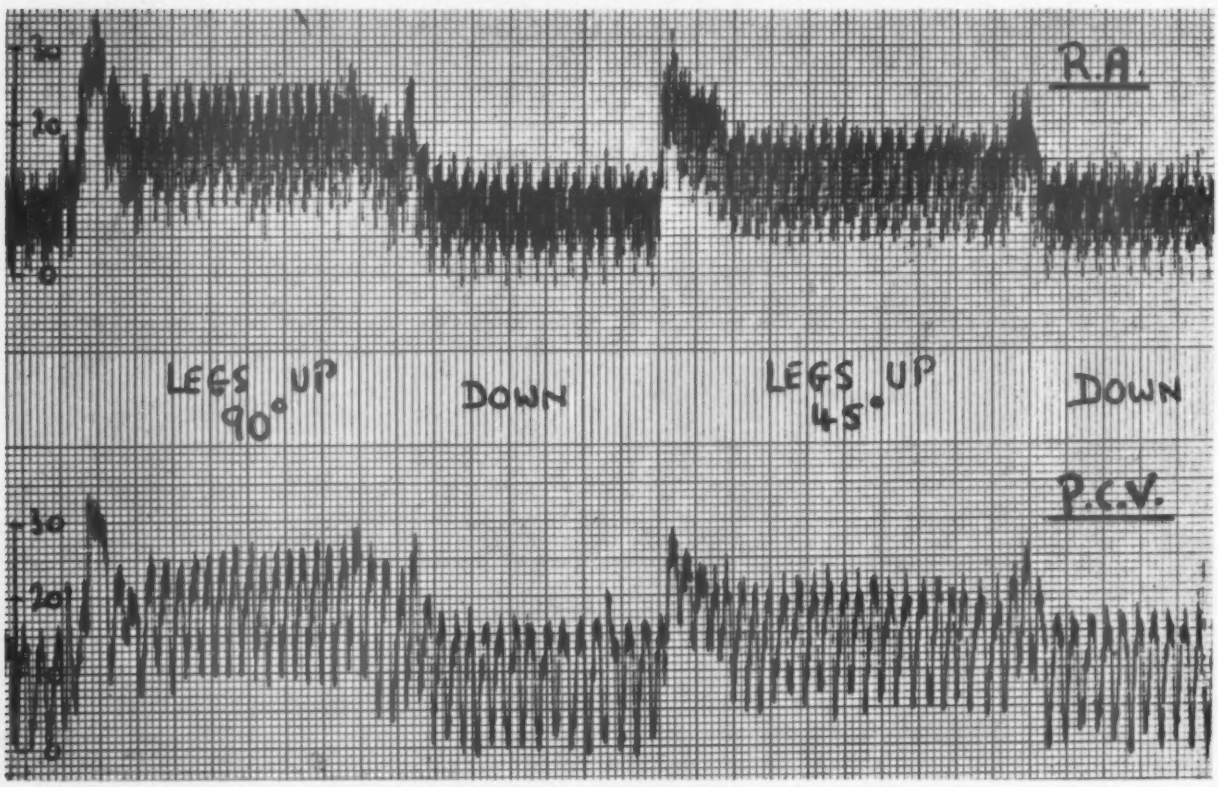

FIG. 10. Left (P.C.V.) and right (R.A.) atrial pressures rising and falling together when the legs are raised and lowered respectively in a patient with constrictive pericarditis.

diagnosis between constrictive pericarditis without calcification and heart failure from an obscure cardiomyopathy can be extremely difficult at times, an attempt was made to reveal some other means of distinguishing between the two. In the following paragraphs the results of some research in this direction are presented.

Atrial Pressure Pulse: The form of the atrial pressure pulse may help. Giant *a* waves, for example, are never noted in constrictive peri-

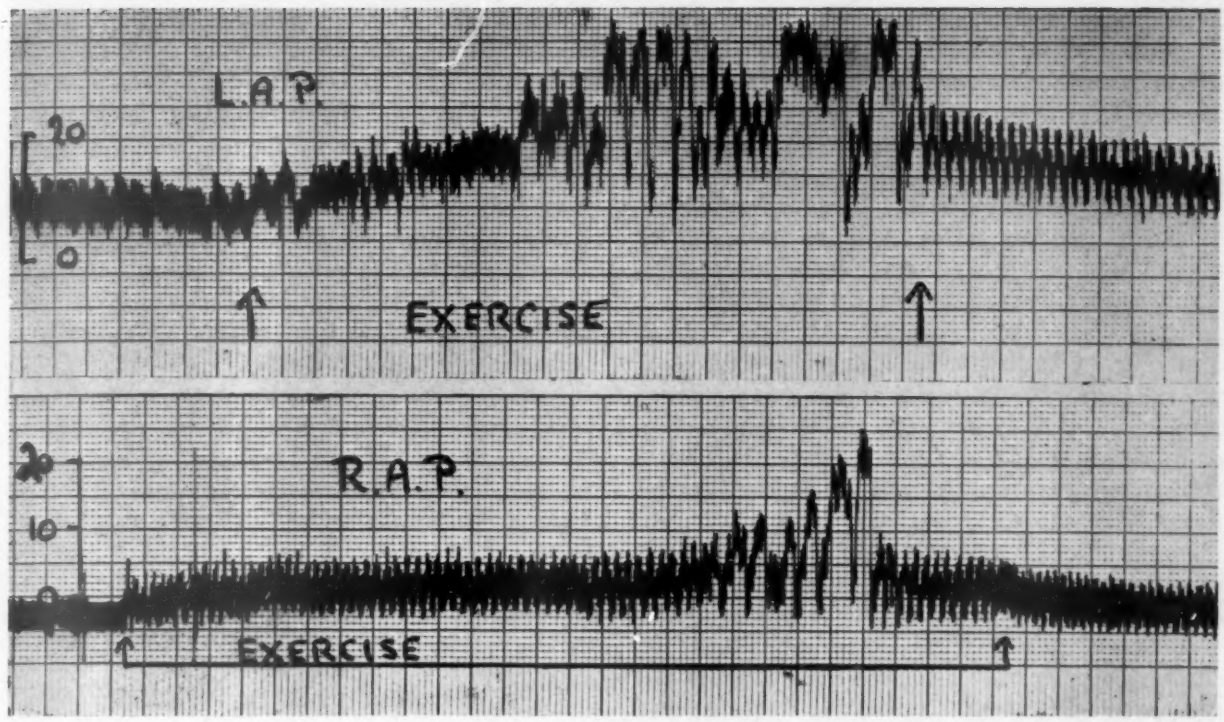

FIG. 11. Further divergence of left (L.A.P.) and right (R.A.P.) atrial pressures on exercise in a patient with cardiomyopathy.

carditis but are common in certain forms of cardiomyopathy when resistance to right ventricular filling may be much increased by gross hypertrophy of the interventricular septum (Bernheim phenomenon). A remarkably sharp *x* descent also seems suggestive of constrictive pericarditis.[14] In my series the *x* descent dominated the venous pulse in only one-sixth of the patients with inactive pericarditis but did so in three-quarters of the patients with active pericarditis. Just how valuable this sharp *x* descent may be in differential diagnosis is yet to be proved.

No reliance can be placed on a conspicuous *y* trough in differential diagnosis as previously mentioned because it is commonplace in cardiomyopathy with heart failure (Fig. 9).

The Relationship Between Left and Right Atrial Pressures: This relationship has proved to be important. In constrictive pericarditis the relationship is usually normal, the left atrial pressure being only a few millimeters of mercury higher than the right (Tables IA and B). The average difference was 2.4 mm. Hg, and the range, −3 to +9 mm. Hg at rest; in only one case was the difference more than 6 mm. Hg and in only two cases was the left atrial pressure slightly lower than the right. On effort, or when the legs were raised passively, the two atrial pressures rose equally together (Fig. 10). In ten cases of cardiomyopathic failure, selected from the general group of cardiomyopathies solely because they were particularly difficult to distinguish from constrictive pericarditis (Table IC), the left atrial pressure averaged 12 mm. Hg higher than the right (range 3 to 21 mm. Hg higher). In three cases only, the difference was within the usual range of constrictive pericarditis. Two of these cases were complicated by severe thromboembolic pulmonary hypertension with pulmonary vascular resistances of 12 and 10 units, respectively. Such a complication would be expected to diminish the left atrial pressure and raise the right atrial pressure. On exercise or raising the legs passively the difference between the two atrial pressures is usually augmented and in milder cases the left atrial pressure may rise conspicuously while the right remains but little affected (Fig. 11).

Cardiac Output: As mentioned previously, the cardiac output was appreciably higher and the A-V difference lower in cases of constrictive pericarditis than in cardiomyopathic failure. The average respective figures were 4.7 and 3.5 L./minute for the output and 51 ml. compared with 75 ml./L. for the A-V difference. The cardiac output was under 4 L./minute in

24 per cent of the constrictive cases and in 80 per cent of those with cardiomyopathic failure; the arteriovenous oxygen difference was under 55 ml./L. in two-thirds of the constrictive cases, but in only one of the ten with cardiomyopathy.

Pulmonary Artery Pressure: Despite the higher output in patients with constictive pericarditis, the pulmonary artery pressure was usually appreciably lower (average 28/15 mm. Hg) than in the patients with cardiomyopathy (average 48/27 mm. Hg). The difference may be expressed more forcibly by stating that the systolic pressure in the pulmonary artery was 40 mm. Hg or more in only 5 per cent of the patients with constrictive pericarditis, and in 80 per cent of those with cardiomyopathy. Again, the pulmonary vascular resistance averaged only 1.7 units in the patients with constrictive pericarditis (range 0.8 to 3.5 units), whereas it was 4 or more units in half the cardiomyopathic cases. Indeed, in two of the latter patients the resistance was extreme at 12 and 10 units, but both of these were complicated by thromboembolic pulmonary hypertension. However, I have two other patients with cardiomyopathy of obscure origin with severe pulmonary hypertension, one with a resistance of 7 units and the other of 14 units; these two patients have not been included in the present series because they could not be confused with constrictive pericarditis. Since a total of only twenty-one of my patients with cardiomyopathy have been catheterized, it is clear that reactive pulmonary hypertension is as common in this group as it is in any other condition that gives rise to critical elevation of the left atrial pressure.

That reactive pulmonary hypertension does not occur with constrictive pericarditis, but does so with the expected frequency in cases of cardiomyopathy, confirms the established fact that the left atrial pressure tends to rise appreciably higher, particularly on exercise, in cardiomyopathy. In constrictive pericarditis passive pulmonary hypertension does not reach the critical level that seems to be necessary to excite a vasoconstrictive reaction. This is attributed to the fact that the right ventricle is hampered as much as the left.

Summary of Hemodynamic Findings: The data are presented in greater detail in Tables IA to C. There was no fundamental difference between patients with active and inactive constrictive pericarditis, although the cardiac output averaged slightly higher (4.8 L./minute) in the patients with inactive pericarditis than in the others (4.5 L./minute). The average A-V difference was the same at 51 ml./L. in each group. The well maintained cardiac output in the patients with chronic inactive pericarditis was all the more remarkable because over two-thirds of them had atrial fibrillation. One might interpret this by postulating that the faster heart rate of atrial fibrillation favored a higher output in constrictive pericarditis. In one subject the cardiac output was measured immediately before, during and immediately after an attack of paroxysmal supraventricular tachycardia at a rate of 170 beats per minute during cardiac catheterization, the rhythm change being provoked by the catheter. The cardiac output, measured simultaneously both by the Fick principle and by the dye dilution technic, rose by about 1 L./minute during the paroxysm. The precise figures by the Fick estimate were 6.3, 7.3 and 6.3 L./minute.

Differential Diagnosis

It may help to sum up the more important points in differential diagnosis between constrictive pericarditis and those forms of cardiomyopathy that may closely simulate it at the bedside (Table II). This excludes the congenital and obstructive cardiomyopathies and those due to obvious causes, such as anemia or myxedema. It does, however, include cases the cause of which may have been subsequently identified, such as amyloidosis, provided the clinical features resemble those of constrictive pericarditis at the bedside. The great majority of these are of obscure origin, both clinically and at necropsy. It is believed that some of the confusion that has surrounded this differential diagnosis has been due to failure to appreciate certain important differences between active and inactive constrictive pericarditis. To emphasize these differences the analysis is summarized in Table II, active and inactive constrictive pericarditis being considered separately.

Favoring a diagnosis of active constrictive pericarditis are a paradoxical pulse, a dominant and sharp *x* descent in the jugular pulse, an early third heart sound, a pericardial T wave pattern on the electrocardiogram and persistent hydrothorax. The early third heart sound and electrocardiographic pattern are, of course, also common to inactive constrictive pericarditis and this diagnosis is favored by atrial fibrillation and pericardial calcification.

TABLE II
Differential Diagnosis of Constrictive Pericarditis and Cardiomyopathy

Finding	Constrictive Pericarditis		Cardiomyopathy (%)
	Active (%)	Inactive (%)	
Paradoxical pulse	50	15	...
JVP*			
Giant *a* (NR†)	...	...	42
Dominant *x* descent	75	17	...
Deep T trough	25	58	Common
Atrial fibrillation or flutter	10	70	33
Left ventricular cardiac impulse	...	10	70
Mitral or tricuspid regurgitation	Rare	Rare	Common
Third heart sound	0.10–0.12 sec.	0.10–0.12 sec.	0.13–0.16 sec.
Electrocardiogram			
Normal	10	16	9
Bundle branch block	...	...	25
Left ventricular preponderance (2–3)	...	...	31
Pathologic Q-T pattern	...	...	6
Pericardial T wave pattern	90	84	29
Roentgenogram			
Pericardial calcification	...	70	...
"Enlargement" (grade 2–3)	Effusion 60	...	87
Hydrothorax	90	Rare	Rare
Catheter data			
LAP‡ minus RAP§	0–6 mm. Hg	0–6 mm. Hg	10–20 mm. Hg‖
Cardiac output			
Average	4.5 L./min.	4.9 L./min.	3.5 L./min.
Under 4 L./min.	25	25	80
Arteriovenous oxygen difference			
Average	51 ml./L.	46 ml./L.	75 ml./L.
Over 55 ml./L.	37	31	90

* JVP = Jugular venous pulse; † NR = Normal rhythm; ‡ LAP = Left atrial pressure; § RAP = Right atrial pressure; ‖ Excluding patients with thromboembolic pulmonary hypertension.

Factors indicating cardiomyopathy are a conspicuous *a* wave in the jugular pulse, a left ventricular cardiac impulse displaced well to the left, mitral or tricuspid regurgitation, a third heart sound falling at its usual time, obvious left ventricular preponderance on the electrocardiogram, bundle branch block (usually left), a pathologic Q wave followed by T wave inversion resembling the appearances of cardiac infarction and conspicuous enlargement radiologically.

On cardiac catheterization, factors indicating both active and inactive constrictive pericarditis are closely similar left and right atrial pressures at rest and on exercise, with a cardiac output over 4 L./minute, an arteriovenous oxygen difference under 55 ml./L. and a pulmonary vascular resistance under 3.5 units. Cardiomyopathy is favored by a left atrial pressure more than 9 mm. Hg higher than the right atrial pressure, an increasing difference between the two atrial pressures on exercise or leg raising, a cardiac output under 4 L./minute, an arteriovenous oxygen difference over 55 ml./L. and a pulmonary vascular resistance of 4 or more units. It should be understood that these observations are valid only when the findings are associated with a high jugular venous pressure and absence of abnormal pressure or volume loads on either ventricle.

Course and Treatment

Patients with active tuberculous pericarditis, already in the constrictive phase, tend to

deteriorate steadily unless relieved by cardiac surgery. A full three months' course of treatment (streptomycin 0.5 gm. twice daily, para-aminosalicylic acid 10 gm. twice daily and isoniazid 100 mg. twice daily) is advised prior to surgical intervention. As emphasized by Andrews, Pickering and Sellors,[21] surgical treatment for constrictive pericarditis should never be withheld on the grounds of active tuberculous pericarditis. Of the seven patients having active pericarditis operated on in this series, the results were excellent in three, good in two and poor in two. None of these patients died. The three patients with active pericarditis in the series who were not operated on died. One of these patients refused operation and the other two cases occurred prior to the time when it was first recognized that surgery was indicated at this stage.

Of the thirty patients with inactive pericarditis, one died before the correct diagnosis was made (1938), eight were treated conservatively, being considered too mild or too old for surgical treatment, and one was seen in consultation at another hospital (fate unknown). The five relatively mild cases have been observed for an average period of five years without material change. Of three elderly patients in the seventh decade when first seen, two are still alive after a period of seven years and the fate of the third is unknown.

Results of Surgery: Pericardiectomy was undertaken in twenty of these thirty patients with inactive pericarditis. The operations were performed by a variety of surgeons including the late Professor Grey Turner, Sir Clement Price Thomas, Sir Russell Brock, Mr. Holmes-Sellors, Mr. Oswald Tubbs and Mr. W. P. Cleland. There were three operative deaths, one prior to the penicillin era. Results were excellent in eleven, good in five and poor in one. This last patient had had a previous pericardiectomy eleven years earlier and died seven years after the second operation. The only other patient in the series that required a second operation subsequently did very well.

Thus, in the whole series the operative mortality was 11 per cent in twenty-seven cases. The results were excellent in 52 per cent, good in 30 per cent and poor or indifferent in 7 per cent. The average follow-up period was four years, discounting two recent cases. Five of the fourteen patients with excellent results have been under observation for seven years and the improvement has been maintained in each. Reconstriction has not been observed. In one patient who had had a limited pericardiectomy some years previously, a second operation showed free cardiac pulsation where a window had been cut out of the thick pericardium, without any suggestion of recurrence.

These results compare favorably with those reported in the literature. A surgical mortality of about 33 per cent until 1946[7] decreased to about 15 per cent in 1951.[22] The results of surgical treatment were good in 62 per cent of the 415 cases reviewed by Chamblis.[22] Good results imply improved cardiac filling and forward flow, considerable reduction of left and right atrial pressures and disappearance of fatigue, dyspnea, ascites and edema. The venous pressure may not be quite within normal limits; however, Kussmaul's sign often remains and the third heart sound may still be heard, although it is usually softer and occurs appreciably later.[23] Normal rhythm is seldom restored, the electrocardiogram is usually unchanged and the x-ray appearances may not be very different.

Summary

1. A series of forty cases of constrictive pericarditis is analyzed and the subject reviewed in the light of this experience.

2. One-quarter of the cases were still in the active stage of disease. The chief differences between these patients and those with chronic inactive pericarditis are emphasized.

3. A paradoxical pulse, a dominant and sharp *x* descent in the jugular pulse, normal rhythm, more than slight enlargement of the heart shadow and persistent hydrothorax were noted more commonly in the group with active pericarditis. Atrial fibrillation, a relatively small heart and pericardial calcification strongly indicated inactive cases of long duration. An early third heart sound and a characteristic electrocardiographic pattern occurred with equal frequency in both groups.

4. In differential diagnosis perhaps the only serious difficulty is in distinguishing constrictive pericarditis from cardiomyopathy of clinically obscure origin. Factors indicating cardiomyopathy are a conspicuous left ventricular cardiac impulse, a third heart sound falling at its usual time, mitral or tricuspid regurgitation, bundle branch block, electrocardiographic changes denoting left ventricular hypertrophy or necrosis and more than slight cardiac enlargement radiologically.

5. In the absence of thromboembolic pulmonary hypertension, the left atrial pressure is usually 10 to 20 mm. Hg higher than the right in cases of cardiomyopathy, the divergence increasing with exercise; in chronic constrictive pericarditis the two atrial pressures usually remain similar under all conditions. The implication that cardiomyopathic heart failure is initially and predominantly left-sided is accepted.

6. The cardiac output averages about 25 per cent lower and the arteriovenous oxygen difference 33 per cent higher in cardiomyopathy than in chronic constrictive pericarditis. The maintenance of a resting cardiac output well over 4 L./minute when there is atrial fibrillation is characteristic of constrictive pericarditis.

7. The absence of reactive pulmonary hypertension in constrictive pericarditis despite resting left atrial pressures in the mitral stenotic range is noted.

8. The operative mortality was 11 per cent in the twenty-seven cases treated surgically. The results were good or excellent in 82 per cent and poor or indifferent in 7 per cent. Reconstriction was not observed. Activity is no bar to successful surgical therapy; none of the seven patients with active pericarditis operated upon in this series died.

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Chronic Constrictive Pericarditis Treated with Pericardiectomy*

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THE OPERATIVE treatment of chronic constrictive pericarditis probably constitutes the first elective surgical procedure in the development of cardiac surgery. The inception of pericardiectomy has been a great stimulus in the development of this surgical specialty. As an operation of historical interest it is unique in that it remains of practical importance today.

Although this operation has been used widely since the early 1920's, there still is controversy among many surgeons who advocate different approaches in the decortication of the diseased pericardium. In spite of the lapse of time and the accumulation of clinical experience, there continues to be dispute as to the correct technic and operative approach. Perhaps more important than that controversy is the frequency of misdiagnosis in those patients who show symptoms of chronic constrictive pericarditis. Patients with the typical features of chronic constrictive pericarditis are still subjected to exploratory laparotomy for nonexistent hepatic disease or extrahepatic obstruction of the venae cavae and hepatic portal systems. It would appear, therefore, that there is more to be done with chronic constrictive pericarditis.

HISTORICAL BACKGROUND

Historical review of the surgical treatment of constrictive pericarditis is not pertinent at this time. A chronologic listing of the authors who have contributed to the operative correction of constrictive pericarditis is an orderly listing of famous surgeons of the past and present generations. It can be stated that a review of the significant papers related to pericardiectomy reveals a running controversy in the matters of appropriate surgical approach and technic; the matters of diagnosis and selection of the surgical candidate have caused little controversy. The real arguments have been confined to the definition of satisfactory pericardial decortication; how the operative procedure should be approached, where it should begin and where it should end. There were, and still are, advocates of the advice of Schmieden and Fischer,[1] and Schmieden and Westermann[2] that decortication should begin in the region of the left ventricle and be followed by relief of constriction of the right ventricle. These viewpoints were championed by Graham, Singer and Ballon,[3] Churchill,[4] Heuer and Stewart,[5] Beck and Griswold,[6] Bigger[7] and others. In 1941, Blalock and Burwell[8] stated that patients with constrictive pericarditis have embarrassment of the right side of the heart and that decortication of the right ventricle should be the logical approach. In succeeding years viewpoints changed constantly. It even was suggested that pericardiectomy might be performed as a two stage procedure, operating first through one side of the thorax and then, at a later date, through the other. In 1949, Holman and Willett[9] introduced the sternal-splitting approach which permitted wide access to the anterior aspect of the pericardium and permitted decortication over the right ventricle, over most of the left ventricle and in particular over the orifices of the superior and inferior venae cavae. Although this seemingly radical approach to the problem of pericardial decortication appeared to be the ultimate, complete acceptance did not result. Many surgeons remain convinced that a unilateral operative approach is still basically correct, and that through this limited opening satisfactory decortication is possible.

EXPERIENCE

Over the past ten years a total of twenty-six patients have been operated upon at the Cleve-

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land Clinic Hospital for the relief of chronic constrictive pericarditis. During this same interval another thirty-two patients have been operated upon for some manifestation of acute or subacute pericarditis. Although the technical problems associated with this second group are not relevant to this presentation, a number of observations have been made that will be referred to in the discussion of the cause of chronic constrictive pericarditis.

Each of the twenty-six patients who comprise this series was operated upon by the author and his associates. The over-all experience seems to parallel that reported by many surgeons during the past decade. There has been considerable variation in operative approach and technic. More important there has been considerable variation in the caliber of results, some of the patients showing early improvement, others a slow, but progressive improvement and a few with questionable or disappointing results. The cause of the disease was not apparent in the majority of patients. It is obvious that this series has little statistical significance. Perhaps the greatest value that the series can offer is a reflection of the changing concepts in the surgical treatment of constrictive pericarditis and in those factors that may have a direct bearing upon the clinical result.

Of the twenty-six patients upon whom pericardiectomy was performed, two died without leaving the hospital and at least seven of these patients have since died. In each case the final cause of death originated in the heart and it can be assumed that either the operation provided little benefit or the initial improvement was transient. Fifteen of the living patients were definitely helped by the surgical procedure.

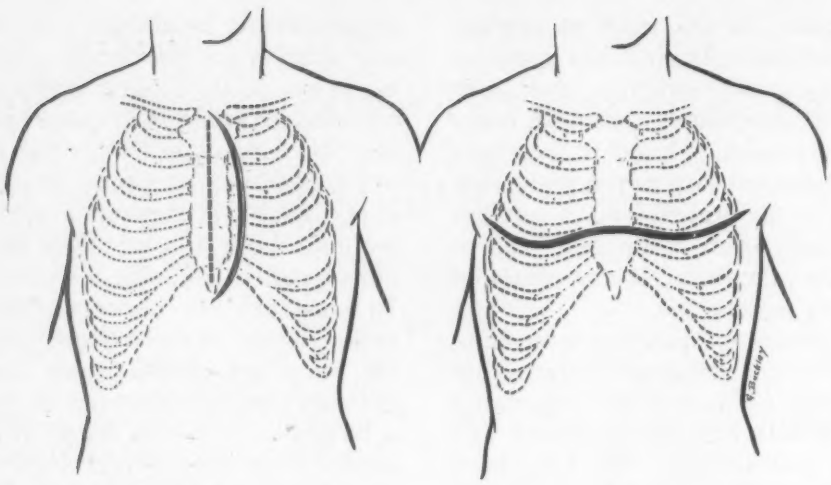
Etiology

Tuberculosis: The diagnosis of chronic constrictive pericarditis implies a tuberculous infection of the pericardium. The relationship between tuberculosis and constrictive pericarditis has been emphasized so often in the literature and in clinical teaching that the majority of students and physicians assume that this relationship is constant. It appears that the incidence of constrictive pericarditis on a basis of tuberculosis is far less than it was originally thought to be. In this series tuberculosis can be indicted in only two of twenty-six patients.

Hemorrhagic Pericarditis: In most of the patients with constrictive pericarditis who come for surgery, no specific cause can be found, although study by culture and histopathologic examination are performed routinely. A finding of particular interest which might have direct bearing upon the cause of the original disease was evident at the time of surgery in most of the twenty-six patients, namely, the presence of residual blood elements within the pericardial sac and in the area of major involvement. In our opinion this finding is extremely significant. In more than fifty per cent of the patients from another series who underwent surgical treatment for acute pericarditis, some element of compression was demonstrated by tamponade, and a bloody effusion was found at the time of operation. In those patients the interior of the pericardial sac resembled the involved pleural space of patients who had recent hemothorax. The frequency of this observation in patients who were treated for pericardial effusion and secondary tamponade suggests that the original process was that of hemorrhagic pericarditis of unknown cause. It is remarkable that culture studies are almost always negative in patients who manifest this process. It is likely that there is a direct relationship between acute hemorrhagic pericarditis with tamponade and constrictive pericarditis with obvious residual blood elements.

The presence of blood in a synovial space such as a joint or a pleural cavity may incite inflammation and stimulate additional effusion. Absorption of the secondary effusion is associated with deposition of fibrin and elements in the blood that form a lining or cortex on the involved surfaces. In the chest this cortex has been referred to erroneously as "thickened pleura." The initial deposit of the elements of the blood and fibrin may be absorbed. Sometimes, however, absorption does not occur; instead there is replacement by fibrous tissue that may eventually cause progressive contraction and thickening in the involved area. Irregular deposits of calcium may develop and ultimately may result in a stony cast of the original collection of fluid.

Blood within the pericardium, particularly in the presence of some initially inflammatory process, may produce the same sequence of reaction that is known to occur within a joint or a pleural space. For this reason it is our belief that chronic constrictive pericarditis may be the end result of unrecognized acute hemorrhagic pericarditis of unknown cause. It has been suggested that acute hemorrhagic pericarditis is viral in origin, as shown by the lack of bac-



A B

FIG. 1. Sketches showing two surgical approaches for adequate pericardiectomy, both of which permit visualization of the anterior aspect of the pericardial sac and its contents. Figure A shows the sternal-splitting incision that may be performed rapidly with an electric saw. The skin incision is made well to one side of the midline. In event of postoperative incisional infection, this method reduces the likelihood of continuity of infection to the bone incision. Figure B shows the sternal-transecting incision which usually involves both pleural spaces. This bilateral thoracotomy need not be symmetric as shown; it may be advantageous to enter one pleural space appreciably higher or lower than the other. This creates an oblique plane of incision rather than a transverse one.

teriologic findings on routine culture studies taken long after the acute process has subsided.

FACTORS THAT CONTRIBUTE TO POOR SURGICAL RESULTS

Many papers on the surgical treatment of chronic constrictive pericarditis have emphasized the importance of the site and extent of pericardial decortication. It has been stated repeatedly that a poor result can usually be attributed to inadequate decortication; however, this is not always the major factor in determining the outcome.

Myocardial Disease: A critical review of our limited series has shown that a number of patients did not obtain ideal results. Several of the patients showed gradual improvement months or even a year after the original operative procedure. In 1941, Blalock and Burwell[8] explained the delayed improvement on the basis of myocardial weakness or atrophy that had occurred before relief of constrictive pericarditis was obtained. In several patients we observed prompt herniation of the weakened myocardium as the constricting membrane was removed, and after decortication was completed there was a large amount of cardiac dilatation. It would seem that myocardial disease would be the logical explanation for this finding. Under such circumstances it seems unlikely that faulty or inadequate decortication would be responsible. There are patients who have obtained considerable initial benefit from decortication only to have myocardial disease develop years later. It is likely that some patients will have both pericardial and myocardial disease; in such patients decortication of the diseased pericardium relieves only one part of the problem.

Inadequate or Difficult Decortication: If the myocardium is reasonably healthy and the surgical result is poor, it must be assumed that decortication was inadequate. The prime requisite of pericardiectomy is adequate exposure. (If the basic exposure is inadequate, decortication will be similarly limited.) The limitations imposed by a unilateral thoracotomy incision will serve to explain the majority of surgical failures.

However, there are other factors that contribute to technical failure. The thickened pericardium and its underlying fibrous cortex may have a peculiar lamination, and decortication may be made in an improper cleavage plane. This may lighten the overlying pericardium without offering true decompression. The ideal decortication will remove the diseased constricting membrane from the underlying epicardium over a sufficient area so that the ven-

tricles can contract and expand normally. In the occasional patient the diseased pericardium with its underlying fibrous cortex and deposits of calcium may actually make inroads into the myocardium itself; in others, a pathologic fusion may occur that does not respect any cleavage plane. When spicules of calcium and fibrous tissue have penetrated the myocardium and its overlying epicardium, surgical decortication becomes almost impossible. Although such instances are uncommon, an occasional patient will have chronic constrictive pericarditis that cannot be corrected surgically.

Postoperative Complications: Postoperative complications that may yield a fatal outcome are always possible, particularly in the patient who has been incapacitated for a long period of time and in whom there has been ample time for peripheral venous thrombosis to develop. Whereas reactivation of the pre-existing inflammatory process is unlikely, it can occur despite the use of antimicrobials and antibiotics.

Technic

The surgical treatment of chronic constrictive pericarditis demands adequate decortication of the diseased pericardium with the least risk to the patient. There will be individual variation as to the evaluation of the patient as a candidate for surgery, and also as to the operative findings (variations that influence the success of the decortication).

Wide exposure of the pericardium is essential for satisfactory operative correction and may be accomplished through a sternal-splitting incision, as advocated by Holman and Willett,[9] or by a bilateral thoracotomy that transects the sternum (Fig. 1A). The sternal-splitting incision is perhaps more satisfactory and is applicable in almost every instance in which pericardiectomy is indicated.

Median Sternotomy or Sternal-Splitting Incision: When properly performed, this incision gives excellent exposure to the entire anterior aspect of the pericardial sac from the diaphragm to the great vessels. The operation may be performed without entering either pleural space, and under certain circumstances this may be a decided advantage during the postoperative period. With an electric saw, sternotomy is quickly performed with little danger of associated traumatic shock. As Holman and Willett[9] have stated, the Lebsche sternal knife, or the hammer and chisel should not be considered. Proper application of the median sternotomy

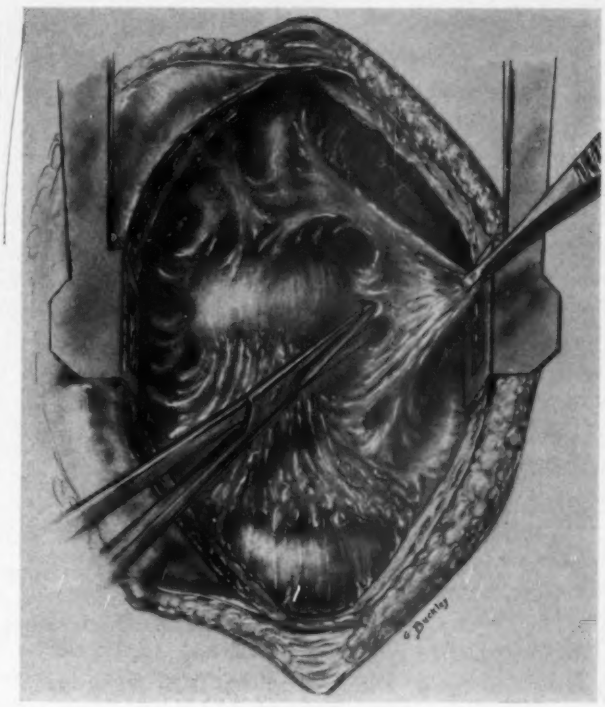


Fig. 2. The conventional rib spreader is utilized to separate the sternal segments after a complete sternal split. The full length incision permits visualization of the entire anterior aspect of the pericardial sac and its contents. The overlying mediastinal fat and thymic remnants must be removed by sharp and blunt dissection to expose the diseased pericardium. Surgical debridement of the anterior pericardial surface should extend from the diaphragm to the level of the sternal notch and from one phrenic bundle laterally to the other.

permits exposure of the pericardial sac from one phrenic bundle to the other.

Some surgeons object to the sternal-splitting incision because of troublesome bleeding and postoperative separation of the wound. Bleeding occurs from the surfaces of the marrow and the periostium. It is likely to occur in the patient with high venous pressure and in the patient in whom there is inflammatory reaction in the anterior mediastinum. Adequate hemostasis may test the patience of the surgeon but it can be achieved. An infrequent complication, but a distressing one to the patient, is postoperative wound infection that may lead to the separation of the sternum. This can constitute a serious problem, as the separation of the sternum produces a major disturbance in the cardiopulmonary physiologic system and permits open infection of the operative site. Although separation of the sternum rarely happens, the possibility does exist in this day of antibiotic-resistant "hospital infections."

Sternal Transection with Bilateral Thoracot-

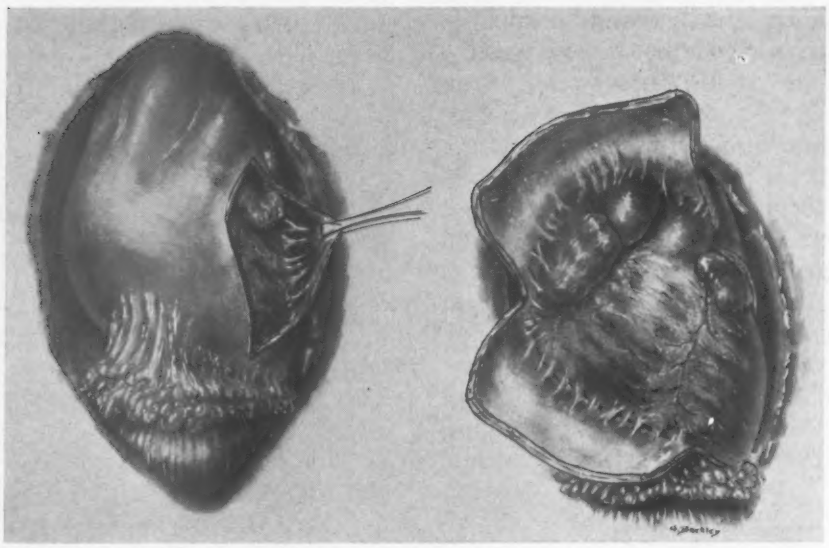


FIG. 3. The decortication of the diseased pericardium which may be performed by a combination of sharp and blunt dissection. In the majority of instances sharp dissection with fine surgical scissors will be preferable to any other method. The initial pericardial incision will be safer in those areas relatively free of disease. Once the cleavage plane has been identified, decortication should be as reasonably extensive as the pericardium and the general status of the patient will permit. Not infrequently there will be localized areas, particularly calcific spots, which must be left behind as residual islets of diseased pericardium. In the majority of cases a decortication that extends across the anterior surface of the heart from one phrenic bundle to the other will afford complete physiologic relief of the compression syndrome.

omy: This incision has received wide application since the development of open cardiotomy that utilizes extracorporeal circulation. Prior to this, however, it was used by a number of surgeons in the treatment of chronic constrictive pericarditis. The incision is cosmetically acceptable, particularly in young women, as it conforms to the submammary creases. It affords excellent exposure of the pericardial sac, permitting access to the lateral aspects of the pericardium extending posteriorly to both phrenic bundles (Figs. 1B and 2).

In the critically ill patient the sternal transection with bilateral thoracotomy has specific drawbacks, as both pleural spaces are traumatized, and associated reduction in the pulmonary function may occur during the immediately postoperative period. Both internal mammary bundles must be divided, promoting the possibility of postoperative bleeding, particularly in the patient with high venous pressure and moderate obesity. The incision is useful, however, in the patient who has already undergone one anterolateral thoracotomy and incomplete decortication.

Technic of Decortication: The degree of success after decortication is influenced by the choice of incision, the character of the pericardium and the underlying myocardium. Despite arguments among surgeons concerning the correct incision for pericardiectomy, the ideal incision provides the best exposure and the least trauma. As stated before, the diseased pericardium may manifest itself in many ways. In some patients the decortication is easy, and the cortex may be readily peeled from the underlying epicardium. More often the involved pericardium is laminated; and if extensive calcification has occurred, the proper cleavage plane is difficult to establish and to maintain. Whether the surgeon uses sharp or blunt dissection will depend upon the immediate findings at operation. When an easy decortication is possible, the procedure should be as extensive as the exposure permits (Fig. 3). Utilizing the sternal-splitting or the sternal-transecting incision the ideal decortication permits removal of the entire pericardium from one phrenic bundle to the other and from the diaphragm to the great vessels. Considering the pericardial sac as a large pod, the anterior half of the pod should be completely removed. If this is accomplished, sufficient release of constriction will occur and a desirable result will be obtained if the myocardium is reasonably healthy.

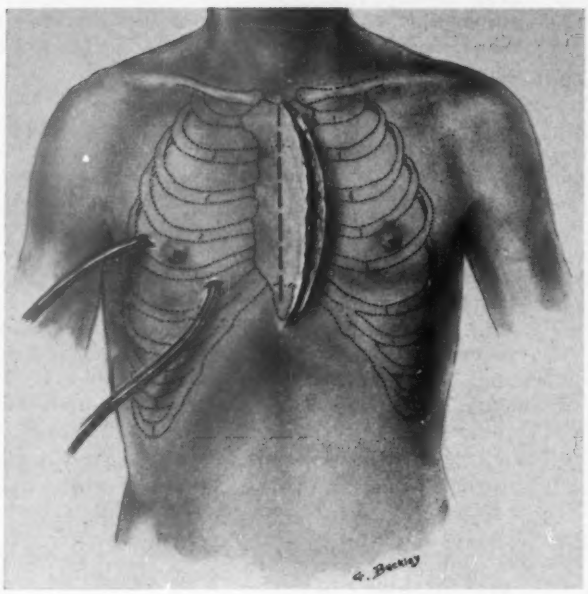


FIG. 4. The correct manner in which surgical drainage of the operative site is accomplished is an extremely important step in the procedure, as failure to provide drainage may permit partial recurrence of the constrictive manifestations and, on occasion, may produce acute postoperative tamponade. Drainage of the anterior mediastinum through the right pleural space by conventional chest catheters provides the safest and most effective postoperative decompression.

It makes little difference whether the decortication begins over the right or the left ventricle, as long as the surgical procedure is accomplished. When extensive calcification is present, or when the diseased process has obliterated any cleavage plane between cortex and epicardium, the decortication may be quite spotty and plaques of disease will be left behind. Under these unfavorable circumstances the outcome of surgery will depend a great deal upon the persistence and tenacity of the operating team.

Discussions concerning the proper technic for decortication have mentioned the advisability of mobilizing both the superior and the inferior vena cava. Usually this is not difficult when either of the previously mentioned incisions have been employed. Although this practice has been followed by the author, at no time has a constricting ring been noted at the points of entry into the pericardial sac; the same may be said for the pulmonary veins.

The surgical procedure may be well tolerated by patients whose decortication is easy, but under less favorable circumstances it may be a trying procedure to the patient and frequent rest periods will be necessary. Local application of anesthetizing drugs such as cocaine, or its synthetic derivatives, have doubtful benefit. The best support for the patient is given by a competent anesthetist who offers adequate oxygenation while maintaining a relatively light level of anesthesia. The extent and the frequency of surgical rest periods may be assessed by direct visualization of the beating heart, observation of the electrocardiographic monitor and the vital signs of the patient.

Closure and Immediate Postoperative Treatment: Drainage (Fig. 4) of the retrosternal space is best accomplished by the use of a catheter and water-seal suction; transpleural drainage, particularly if one or both pleural spaces have been entered, may be most effective. Closure of the incision after decortication may be a tedious, time-consuming task. Meticulous hemostasis must be obtained, particularly in that patient who has had chronically high venous pressure. This care is emphasized, as postoperative bleeding may have great bearing on the final result. Closure of the sternal wound, whether split or transected, is best accomplished with braided steel sutures. Single-strand steel sutures are prone to early fragmentation.

Postoperative serosanguineous effusion may be profuse during the early postoperative hours. Care must be taken to distinguish between effusion and postoperative bleeding. As stated before, postoperative hemorrhage must be anticipated in the more difficult operations in patients who have had long-standing high venous pressure. When postoperative bleeding persists, a second operation may be mandatory.

SUMMARY

During the past ten years twenty-six patients have been operated upon at the Cleveland Clinic Hospital for the surgical correction of chronic constrictive pericarditis. There has been considerable variation in technical features of the operation, but with increasing experience the trend is toward one of two basic incisions: (1) the median sternotomy (sternal-splitting) or (2) the transverse sternotomy (sternal transection). Either incision provides excellent exposure of the anterior aspect of the pericardial sac and its contents.

Successful decortication is dependent upon the surgical exposure; however, other factors may be of equal significance. The most important of these is the character of the pericardial disease in the patient. The ability to establish a cleavage plane is usually dependent

upon the pathologic process itself. Other reasons for failure are myocardial disease and postoperative complications.

The cause of chronic constrictive pericarditis is still a matter of interest. Although tuberculous pericarditis was originally presumed to be the responsible cause of constrictive pericarditis, it now appears that this may be comparatively rare. Comparison of a sizable series of patients with acute pericardial effusion treated during the same time interval suggests a possible relationship between acute hemorrhagic pericarditis and chronic constrictive pericarditis. The investigative problem remains to establish the common cause of acute pericardial hemorrhage and the factors that allow intrapericardial blood to incite a possible constrictive pericarditis.

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Pericarditis Complicating Myocardial Infarction*

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AN EXTRAORDINARILY accurate account of the pertinent clinical features of that type of pericarditis which accompanies myocardial infarction was recorded as early as 1872.[1] At first the etiology and full significance of this lesion was not appreciated.[2,3] However, in the interval from 1892 to 1910 its relationship to coronary occlusion was clarified.[4] In the course of reporting two cases and correlating the clinical manifestations with the pathologic findings Maximilian Sternberg[5] suggested the term "pericarditis epistenocardia." In short order, thereafter, numerous references to the condition appeared in the mounting reports on the symptomatology of ischemic heart disease and coronary occlusion.[6,7]

PATHOLOGIC CONSIDERATIONS

At autopsy pericarditis is variously found in 30 to 80 per cent of patients with myocardial infarctions.[5,9] In most instances the involvement is highly localized. However, the zone of inflammation may extend through the entire pericardium.[10,11] As a rule, with recent infarcts the pericarditis is characterized by a dry, fibrinous, sterile exudate which overlies the area of necrosis.

The occasional large effusion which develops is encountered only when the pericarditis is very extensive. Older healed infarcts are covered with a pearl gray patch of scar tissue.

A myocardial infarction must extend to the epicardium if pericarditis epistenocardia is to result. This commonly is the case when the infarct involves the apex. This area is composed of two relatively thin layers, namely, the superficial sinospiral and the superficial bulbospiral muscles. Any involvement of the myocardial wall readily extends through its entire thickness from endocardium to epicardium, thus predisposing to the development of not only pericarditis but a mural thrombus as well.

CLINICAL CONSIDERATIONS

Frequency and Time of Onset: Although it is difficult to judge the frequency with which pericarditis is recognized in patients suffering from a myocardial infarction, it is quite apparent that the clinical is less frequent than the postmortem detection. Many issues contribute to the hesitancies and oversights. Of greatest significance is the fact that the subjective manifestation of pain due to pericarditis cannot be absolutely distinguished from that of myocardial infarction, coronary insufficiency, pulmonary disease or congestive failure. To compound this difficulty the most easily recognized objective sign of pericardial involvement, namely, the friction rub, is not thoroughly reliable in its appearance.

In over 80 per cent of the patients afflicted, pericarditis occurs between the onset of the second and the completion of the fourth day following myocardial infarction. Occasionally, the complication is recognized on the first day. However, it rarely if ever is detected after the tenth day.

As indicated, when the pericardial involvement arises early in the disease and produces pain, this complaint cannot be differentiated with confidence from that of the basic illness. Only on those occasions when chest discomfort is quite piercing in quality is its true pericardial origin suspected. There is every reason to expect, however, that even when obscured and unrecognized, the pain of pericarditis adds considerably to the total clinical disability.

Friction Rub: A pericardial friction rub is audible in approximately 20 per cent of patients with myocardial infarction.[12,13] Never is it

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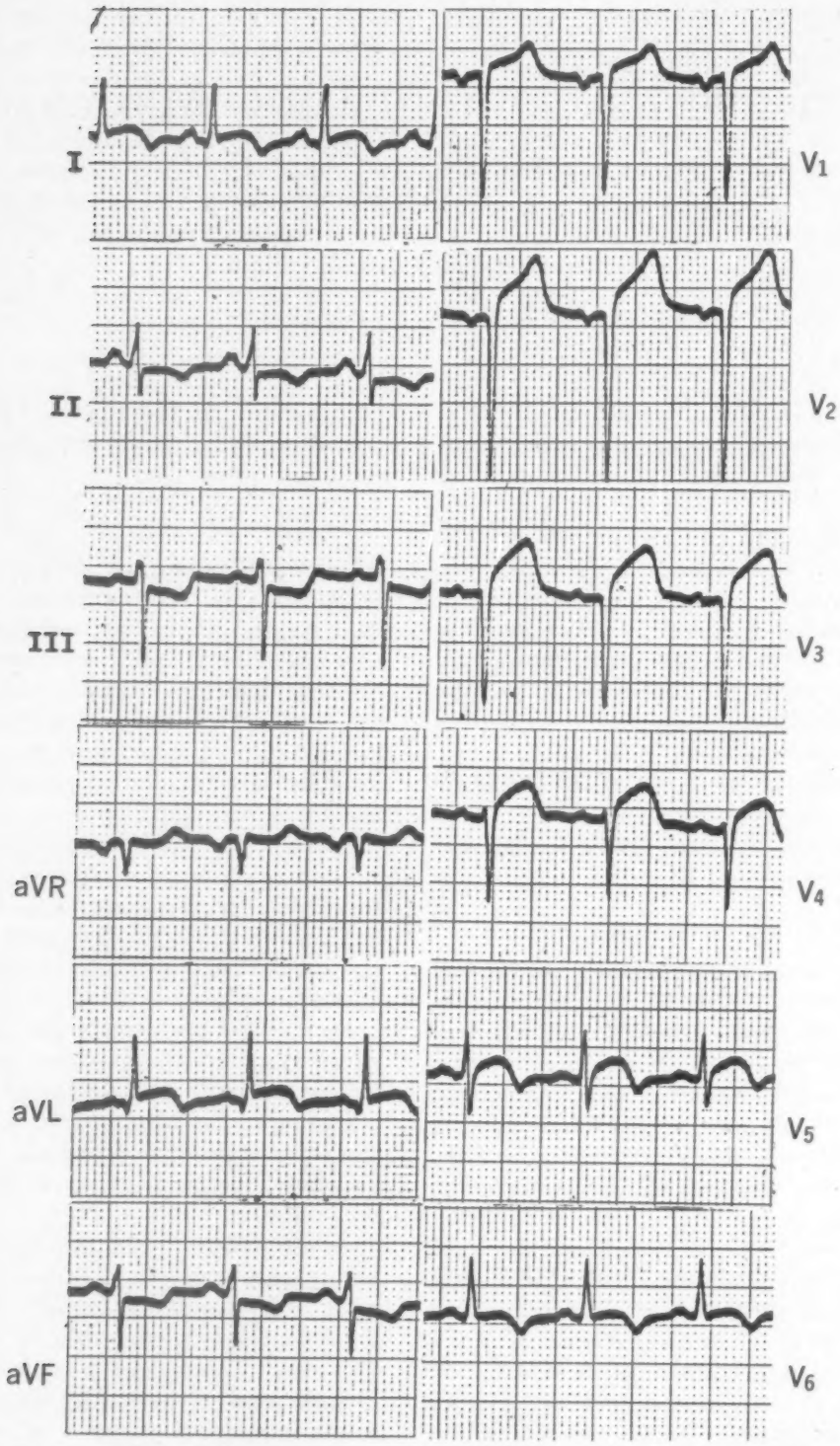

FIG. 1. Marked RS-T segment elevations encountered in anterior infarction. These were accompanied by the physical findings of pericarditis. The difficulty of differential diagnosis between segment alterations due to myocardial infarction and those of the pericarditis is self apparent.

heard until twenty-four hours after the onset of the basic disease since at least that length of time is required for the extension of the pathologic process to the epicardium. It may be inaudible in certain instances because of the poor contractile properties of the injured myocardium. The duration is transitory. In most cases the rub disappears between the first and second

examination. On rare occasions it may persist for as long as two weeks.

The *location of the rub* usually is in the region of the lower portion of the left ventricle. Most commonly it is heard to the median side of the apex or on either side of the lower end of the sternum. Rarely, is it limited to the basal region. Occasionally, a friction rub is audible in the usual areas of the anterior chest even when the actual pericarditis is located over the posterior or diaphragmatic walls of the heart.

The *extent of the rub* is almost always limited to an area not more than 5 or 6 cm. in diameter. This may increase as the complication progresses until the sound is audible over the entire precordium.

Pericardial Effusion: It is not likely for this type of pericarditis to be accompanied by a detectable or compressing effusion since the tissue involvement is quite limited. When it does appear, the effusion may be serous or serosanguineous.

A frank hemopericardium is a consequence of cardiac rupture or a complication of anticoagulant therapy. The latter is more apt to occur with large infarcts. It should be suspected in any patient in whom during the course of anticoagulant therapy, rapid cardiac enlargement, a persistent friction rub, a fall in hemoglobin, renewed fever and leukocytosis develop.

Electrocardiographic Diagnosis: The criteria for the electrocardiographic diagnosis of pericarditis which complicates myocardial infarction was first established by Barnes.[14] He pointed out that the reciprocal relationships between the RS-T segments and between the T waves in the bipolar leads I and III were replaced by a uniform elevation of the segments and at a subsequent date by a uniform inversion of the T waves. Information was gradually extended to include the diagnostic importance of these changes in association with various depolarization wave alterations in the bipolar limb and unipolar precordial leads[15] (Fig. 1).

The major electrocardiographic clues are considered to be: (1) the absence of discordant RS-T deviations; (2) the "TN" pattern or T wave inversion in bipolar limb leads I, II and III; and (3) transient RS-T segment elevations in all leads accompanying a pattern otherwise typical for anterior or posterior infarction. However, currently it is well recognized that the electrocardiographic diagnosis of pericarditis complicating infarction may be difficult if not impossible. This may be due to the fact that the pericarditis most commonly is limited to the area of infarction and is too small to affect the electrical pattern appreciably. In many other instances the transmural death of tissue abolishes the electrical activity subjacent to the pericardial involvement. Finally, there is always a great reluctance to attribute a monophasic wave to a local or a diffuse pericarditis rather than to a recent myocardial infarction which is known to have occurred.

Therapeutic and Prognostic Considerations

Therapy: No specific therapy is available or indicated for pericarditis which accompanies coronary occlusion. Symptomatic relief is readily attainable with ordinary analgesics. Since large troublesome effusions seldom develop, aspiration of the pericardium is not required.

Corticosteroids have been advised in those instances in which the pericardial reaction has been most extensive and for considerable subjective discomfort. Under these circumstances the synthetic anti-inflammatory steroids are most effective and their use is not complicated by hazardous increased sodium retention.

The presence of an epistenocardiac pericarditis may have a considerable influence on anticoagulant therapy. In all likelihood the presence of a highly localized friction rub for a very transient period during the course of an infarction is not a contraindication to continuing anticoagulation. However, a diffuse rub which accompanies a large infarct or a known myocardial aneurysm represents a distinct deterrent to the continuation or institution of this type of treatment. Anticoagulants should also be withdrawn in those patients in whom pericarditis is accompanied by an effusion in order to avoid a tamponading hemopericardium.

Prognosis: It is not likely that pericarditis itself has any bearing on the prognosis of myocardial infarction. It does reflect, however, on the magnitude of the lesion since a transmural involvement is invariably present. In the vast majority of instances no lasting ill effects develop as a result of pericarditis.

Postmyocardial Infarction Syndrome

Pericarditis epistenocardia must be differentiated from the pericarditis which forms an integral part of the so-called postmyocardial infarction syndrome.[16] The clinical features of

the latter condition include fever, chest pain, evidence of pericarditis, pleurisy and pneumonitis, all of which have a tendency to recur.

The postmyocardial infarction syndrome actually is readily distinguished from pericarditis epistenocardia. It arises at least two and as long as eleven weeks after the clinical infarction. The hallmark of the condition is pain which generally precedes the actual onset of temperature elevation. The pain varies in nature from a severe crushing type to a persistent dull ache. It may persist for as long as several weeks. The pain generally is localized in the substernal area and in the precordium. It may, however, be referred to both sides of the neck, shoulders and arms.

The temperature elevation as a rule averages from 101° to 102°F., with occasional peaks of higher elevations. This temperature elevation may coincide with the initial rise following myocardial infarction, but generally extends beyond that period causing a continuing plateau.

The friction rub heard in the postmyocardial infarction syndrome generally is quite loud and persistent. Finally, unmistakable signs of effusion usually develop.

The etiologic factor in the postmyocardial infarction syndrome is entirely unknown. Although the clinical state is benign, it provokes a measurable discomfort and disability which persist at a time when the clinical manifestations of the basic illness have abated. It is this time element mainly that permits a differential diagnosis without too much difficulty.

Summary

Pericarditis accompanying myocardial infarction is a benign condition with few clinical manifestations. It is incidental to a transmural infarct and, aside from this, anatomic correlation is not significant prognostically. Since the essential clinical feature of a rub is evanescent, many occurrences are probably unrecognized. Treatment is essentially asymptomatic and pericardial aspiration is rarely needed. Anticoagulant therapy should be stopped if there is evidence of diffuse pericarditis or effusion to prevent hemopericardium.

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The Postpericardiotomy Syndrome*

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THE POSTPERICARDIOTOMY syndrome is a delayed pericardial and sometimes pleural and pulmonary reaction that follows surgery in which the pericardium is widely incised. The precise mechanism of production of the syndrome remains in doubt, but the clinical manifestations are more readily recognized and are less confusing now than when they were first widely encountered following surgery on the mitral valve.[1–3] Then there was speculation whether this "postcommissurotomy" or "postvalvulotomy" syndrome represented reactivation of rheumatic fever. Equally in doubt was the appropriate treatment for the complication. In 1958 Ito, Engle and Goldberg[4] pointed out that an identical postoperative reaction occurred in patients undergoing surgery for nonrheumatic heart disease and the feature common to both patients with and without rheumatic heart disease was wide incision of the pericardium. The syndrome was not related to the specific surgical maneuver involved since it developed alike in cases in which the intrapericardial procedure consisted of opening a cardiac chamber, vessel or valve, or pericardiotomy alone in exploration for what proved to be an inoperable condition. The term "postpericardiotomy syndrome" was proposed as the designation for this condition.

Postpericardiotomy Syndrome in Open Heart Surgery: At the time of that report, patients undergoing cardiac surgery utilizing extracorporeal circulation were excluded from the analysis because of insufficient experience with the technic and the apprehension that there might be factors influencing a febrile reaction in these patients other than opening the pericardium for cannulation of the venae cavae and operative repair. They were noted to be febrile postoperatively for longer periods (usually the first week) than patients undergoing "closed" cardiac procedures. However, additional experience has demonstrated that, aside from this difference in the early postoperative period, in patients undergoing pericardiotomy and cardiac surgery involving the heart-lung machine the late postoperative complication known as the postpericardiotomy syndrome develops just as in the previously reported cases. Table I shows the incidence of the syndrome among 100 consecutive survivors of open heart surgery, performed for repair of atrial and ventricular septal defects and for relief of pulmonic and aortic stenosis. The aortic stenosis was rheumatic in origin in at least six patients who underwent mitral valvoplasty at the same operation. One child underwent pericardial exploration and aortotomy only when a common truncus arteriosus rather than an aortic septal defect was identified. We still have not observed the syndrome in a patient whose cardiac operation did not include pericardiotomy.

SYMPTOMS AND SIGNS

Fever around 39°C., generally appearing in the second or third week after the operation, is usually the first manifestation. The fever may merge with the early postoperative temperature elevations so that the patient has a prolonged febrile course, but more often the fever recurs as a delayed reaction after a distinct afebrile period (Tables II and III). The longest interval between operation and first recognized episode of the postpericardiotomy syndrome was four and three-quarter months (patient L. N., whose case report follows later).

Chest Pain: Fever may be the only symptom in the infant and child too young to complain of chest pain, the next most common symptom. The pain is no different from the discomfort characteristic of pericardial involvement from any other cause: precordial or substernal in location, radiating to the left shoulder posteriorly and often aggravated by deep breathing or lying down. Sometimes the pain is referred

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TABLE I*

Incidence of Postpericardiotomy Syndrome According to Age and Lesion in 100 Consecutive Survivors of Open Heart Surgery

Age (yr.)	ASD		PS		VSD		AS		EXP.	
	Op.	PPS	Op.	PPS	Op.	PPS	Op.	PPS	Op.	PPS
<5	5	0	6	2	5	2	...	...	...	...
6–10	12	2	7	1	4	2	...	...	1	0
11–20	17	4	5	1	4	1	...	...	...	...
21–30	8	4	1	3	...	...	2	1	...	...
31–40	5	2	1	0	...	...	4	1	...	...
41–40	2	1	1	0	...	...	6	2	...	...
51>	1	0	1	0	...	...	2	1	...	...
Total	50	13	22	7	13	5	14	5	1	0

* Legend of this and subsequent tables:
Op. Operations.
PPS Postpericardiotomy syndrome.
ASD Atrial septal defect.
PS Pulmonary stenosis.
VSD Ventricular septal defect.
AS Aortic stenosis.
EXP. Intrapericardial exploration.

to the abdomen. Tenderness on precordial pressure may be noted. A nonproductive cough, occasional difficulty in swallowing, fatigue and myalgia or arthralgia may be present.

Signs of pericardial and sometimes pleural or pulmonary involvement can usually be demonstrated by physical examination, roentgenograms and/or electrocardiograms. The pericardial friction rub tends to be fleeting. It could probably be heard at some time in all patients, but in our experience it is detected in about half. Muffling of the heart sounds, paradoxical pulse or cardiac tamponade as signs of pericardial effusion are less common, although enlargement of the cardiac silhouette on the roentgenogram is almost always present.

X-ray Signs of Pericardial Effusion: Often it is difficult to tell whether this enlargement is cardiac or pericardial or both. Helpful radiologic signs of pericardial effusion, present singly or in combination in some patients, include the visualization of a double density of cardiac shadow within a distended pericardial sac (Fig. 1) or the appearance of a fuzzy outline to the large "cardiac" silhouette, and the change in configuration in the supine and upright positions as the fluid shifts. On fluoroscopy

TABLE II*

Characteristics of Fever in Initial Episode of Postpericardiotomy Syndrome in Thirty Patients among 100 Consecutive Survivors of Open Heart Surgery

Lesion	Continued, Prolonged	Recurrent in Hospital	Recurrent at Home	
			Readmitted	Not Readmitted
13 ASD	2	5	6	0
7 PS	3	3	0	1
5 VSD	3	2	0	0
5 AS	3	2	0	0
Total	11	12	6	1

* See footnote to Table I for explanation of abbreviations.

TABLE III*

Time of Onset of Recurrent Fever†

Lesion	1st Week	1 to 2 Weeks	2 to 3 Weeks	3 to 4 Weeks	>1 Month
ASD	0	6	2	1	2
PS	0	1	2	1	0
VSD	0	2	0	0	0
AS	0	1	1	0	0
Total	0	10	5	2	2

* See footnote to Table I for explanation of abbreviations.

† Exclusive of 11 patients whose febrile illness merged with early postoperative fever.

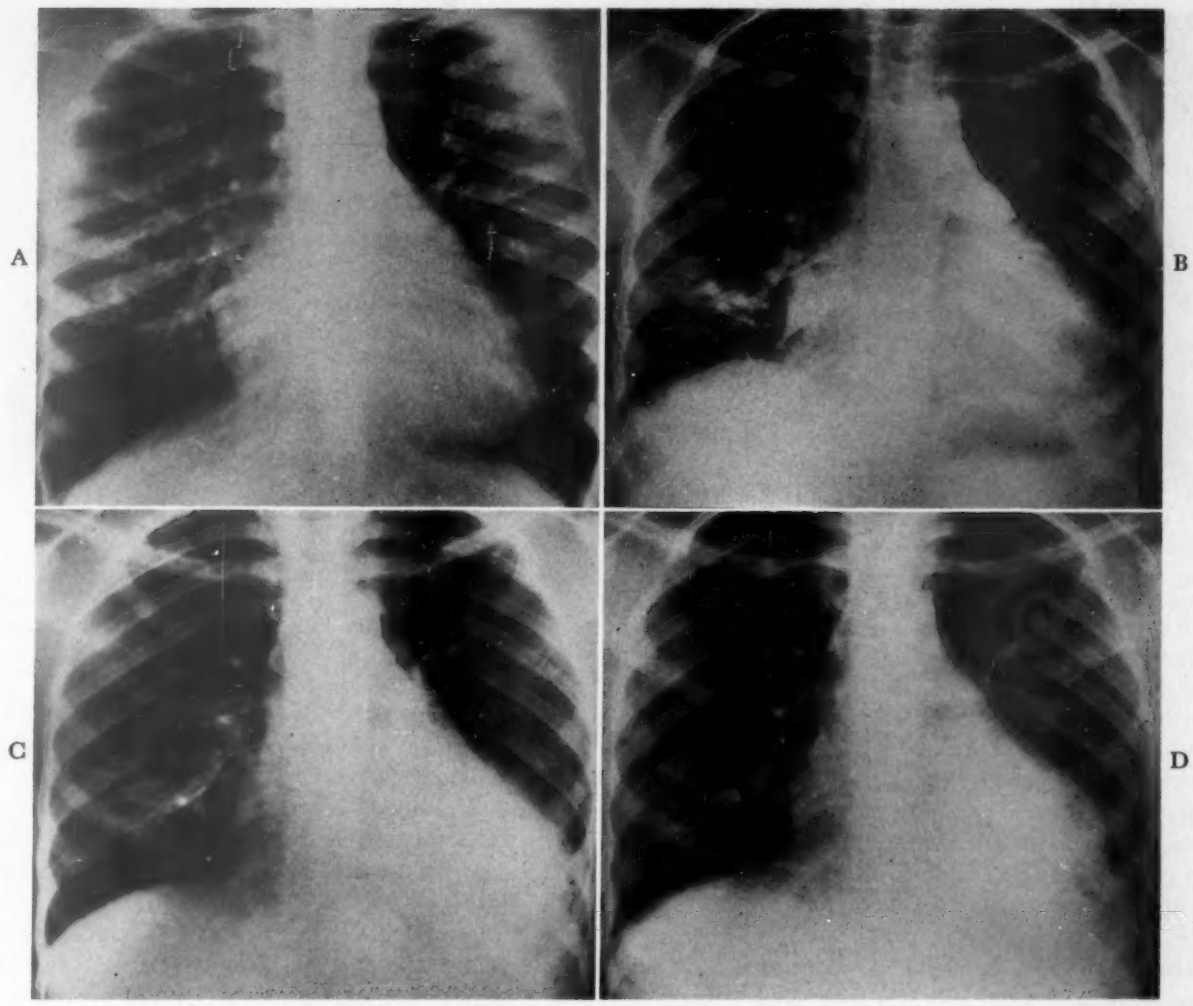


FIG. 1. L. N., nine and one-half years of age. Coronary artery—right atrial fistula. Operation on March 24, 1959. A, preoperative film on March 2, 1959. Note prominence of irregularity of right atrial margin. B, April 6, 1959, prior to discharge. Residual signs of traumatic pericarditis and of atelectasis on the right side. No pleural effusion. C, August 14, 1959, postpericardiotomy syndrome. Note enlargement of "cardiac" shadow with hazy border at apex blending with pleural effusion on left. Distended pericardial sac is clearly seen lateral to aortic knob and main pulmonary artery at upper left heart border. Minimal residual atelectasis on right. D, August 21, 1959, spontaneous regression of pericardial and pleural effusions. Electrocardiographic improvement in S-T segment and T wave abnormalities paralleled the radiologic clearing.

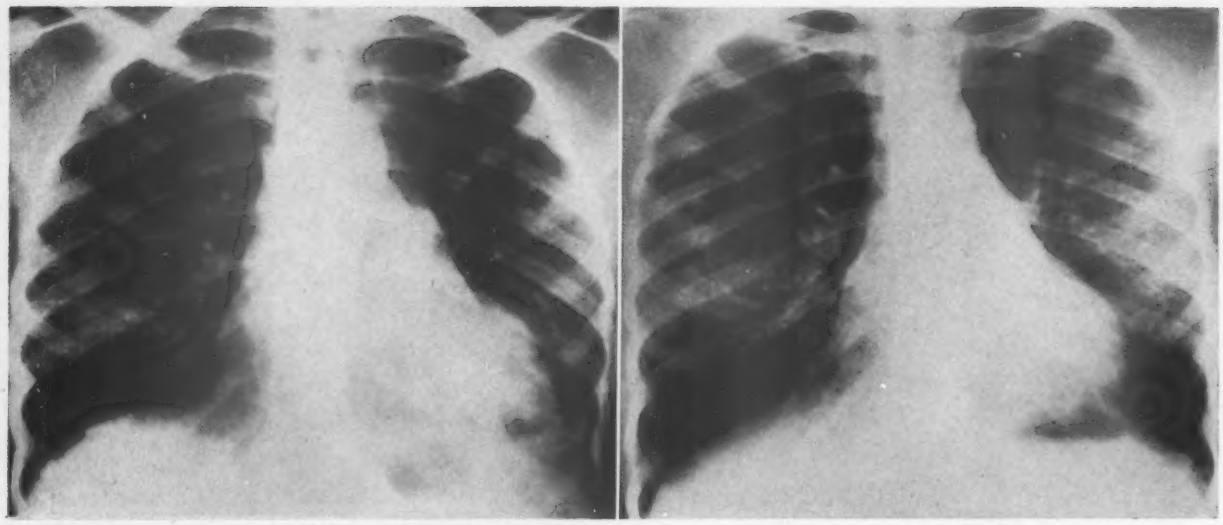
one may observe damped pulsations of the anterior and lateral cardiac borders. If necessary, radiologic proof of the presence of pericardial fluid may be provided by pericardiocentesis followed by injection of air into the pericardial sac, or angiocardiographic demonstration of a homogeneous density outside the cardiac chambers.

Electrocardiograms: When the syndrome is suspected, one of the most useful signs of pericardial involvement has been electrocardiographic: the changing pattern of S-T segments and T waves that characterize the development and resolution of pericarditis.[5] These changes may be masked or difficult to interpret, however, in the digitalized patient or the patient who is left with a conduction disturbance after the cardiac surgery (e.g., right bundle branch block following closure of a ventricular septal defect).

Leukocytosis of 10,000 to 30,000 white blood cells per cu. mm. and elevated sedimentation rate are nonspecific indicators of the inflammation. Blood cultures are negative.

INCIDENCE

The postpericardiotomy syndrome has been reported to occur in 10 to 40 per cent of patients undergoing surgery for rheumatic heart disease. Among patients with congenital cardiac anomalies, we reported in 1958 on thirteen patients



E F

FIG. 1. E, June 15, 1960, recurrence of postpericardiotomy syndrome with pericardial effusion only in this attack. Note shadow of aortic knob and main pulmonary artery visible within shadow cast by distended pericardial sac, and the bulging appearance of the apex of the heart due to accumulation of pericardial fluid. F, June 8, 1960, clearing of pericardial effusion. Size and configuration of heart normal. Return to normal of electrocardiogram also.

with the syndrome among twenty-four with intrapericardial procedures. Subsequent experience with the first 100 patients surviving open heart surgery utilizing the heart-lung machine revealed that the syndrome developed in thirty (Table I). Two of three other children with intrapericardial procedures not requiring the pump oxygenator manifested this complication. Swan and his co-workers[7] in 1959 analyzed the first 100 cases of open repair of atrial septal defects with the patient under hypothermia and noted the syndrome in at least fifteen patients and perhaps in milder form in another five. Johnson[8] over a three year period observed the syndrome in eleven patients with congenital heart deformities but did not state the total number of operations involved.

TABLE IV*

Duration of Initial Episode in 30 Patients with Postpericardiotomy Syndrome Among 100 Survivors of Open Heart Surgery

Lesion	<1 Week	1 to 2 Weeks	2 to 3 Weeks	3 to 4 Weeks	>1 Month
13 ASD	2	5	2	0	4
7 PS	0	2	2	3	0
5 VSD	1	1	2	1	0
5 AS	2	2	0	1	0
Total	5	10	6	5	4

* See footnote to Table I for explanation of abbreviations.

The incidence is probably of the same order of magnitude in patients with congenital and acquired heart disease.

The incidence of the complication after a second operation is unknown. Four of our patients with congenital heart disease underwent a second intrapericardial operation one or more years after the first procedure. It is of interest that in one patient the complication developed after both operations, in the second it did not develop after either operation, the third showed signs of the syndrome after the first but not the second operation, and the fourth patient had no complications after the first operation but on the second occasion the syndrome did develop.

Course: The illness is self limited. It varies in severity and duration, from a brief malady that appears as a fever of unknown origin to a more prolonged and intense reaction with an acutely ill and uncomfortable patient who may manifest signs of congestive failure or cardiac tamponade. Among the hospitalized patients there was good agreement among the various signs of pericardial involvement as the illness subsided; the patient's symptomatic improvement was reflected by a return to normal of the temperature and white blood cell count, followed by the electrocardiogram and chest roentgenogram. Utilizing these five features to determine duration of illness, we found that the initial episode of the syndrome lasted one to two weeks in half of the patients and three to four weeks in most of the others (Table IV).

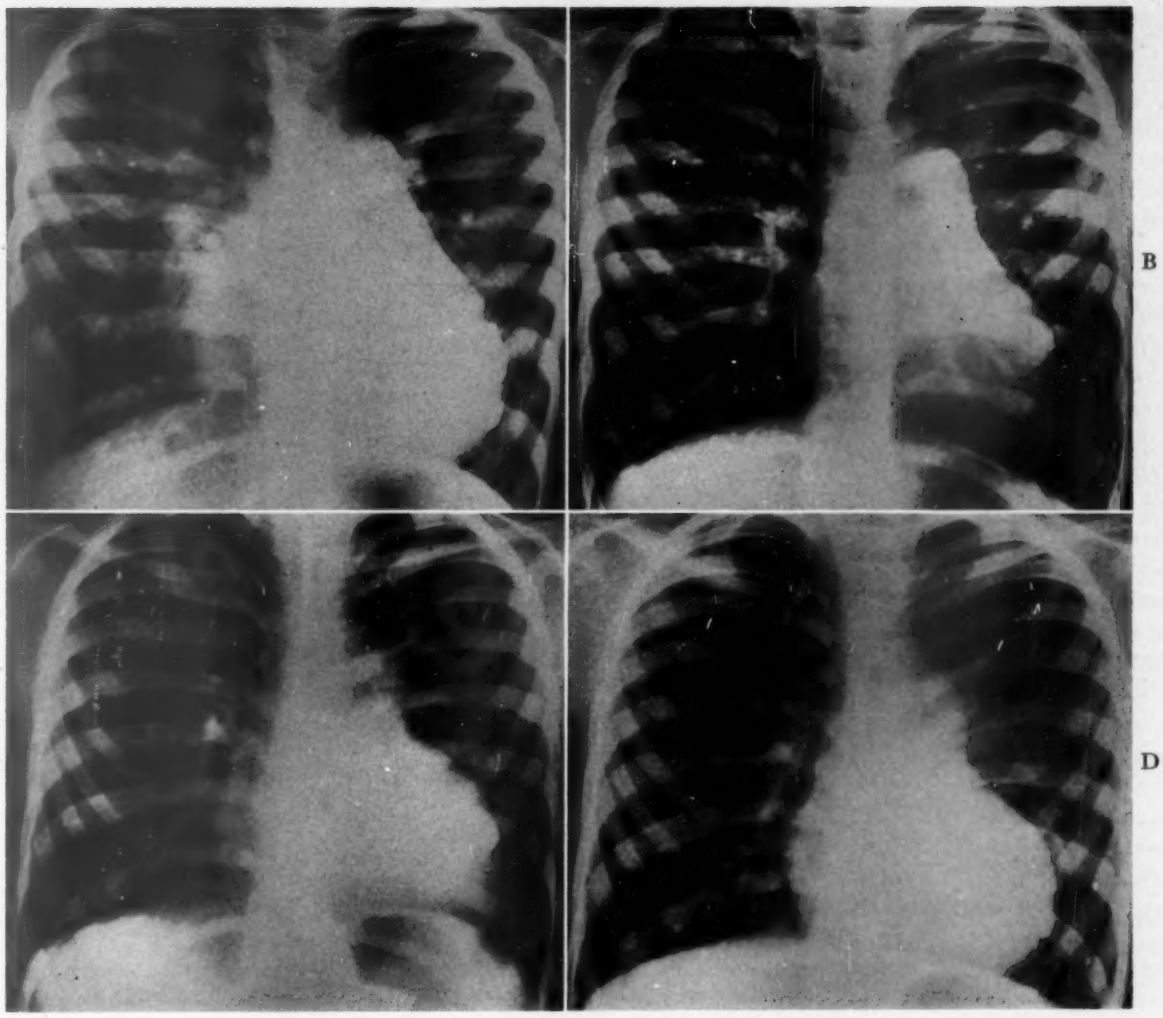


FIG. 2. D. J., eight years of age. Ventricular septal defect with pulmonary hypertension (50/19 mm. Hg). Operation on October 30, 1958. A, Preoperative film on October 29, 1958. Note cardiomegaly and prominence of main pulmonary artery and the engorged branches throughout the lung fields. B, December 15, 1959, fourteen months postoperatively on admission for cardiac catheterization, which revealed normal pressures and no arterialization of blood in right side of heart and pulmonary artery. Note residual prominence of main pulmonary artery but normal vascularity in lung fields, and the striking decrease in heart size. C, June 15, 1960, twenty-one months postoperatively. Postpericardiotomy syndrome, mild. Increase in "cardiac" size. Area below apex of heart is filled in. No pericardial effusion. D, July 8, 1960, spontaneous clearing of pericardial effusion. Electrocardiogram became normal on July 11, 1960, and cardiac silhouette returned to previous size.

Two patients had recurrences of the syndrome, not requiring hospitalization, in four to six months after operation. Another child was readmitted because of a recurrence twenty-two months after repair of a ventricular septal defect (Fig. 2). A fourth patient was hospitalized because of a recurrence fifteen months after ligation of a coronary arteriovenous fistula (patient L. N., described later). Higher recurrence rates have been reported. For example, Larson[6] reviewed 137 survivors of mitral valve commissurotomy and found that fifty-one patients had had seventy-eight attacks.

DIAGNOSIS

Diagnosis of the postpericardiotomy syndrome is based on an awareness of the condition in patients undergoing intrapericardial surgery. It is made both by exclusion of other causes of a febrile illness with chest pain in such a patient and by the search for one or more symptoms and signs of pericarditis. Bacterial endocarditis is the most important condition to exclude by repeated blood cultures. Other conditions considered in the differential diagnosis have included carditis, myocardial infarction, pneumonia, pulmonary infarction, esoph-

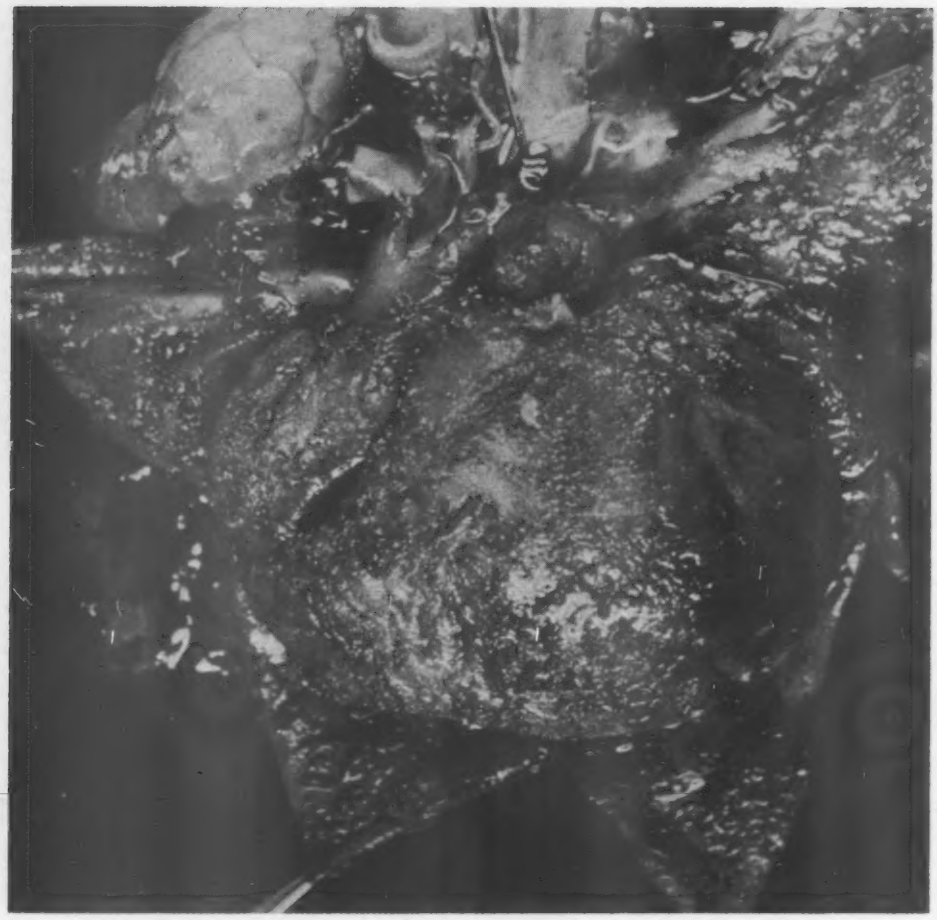


FIG. 3. P. D., six months of age. Pulmonary banding operation on March 31, 1960. Postpericardiotomy syndrome. Death on April 13, 1960. Note intense pericardial reaction on surface of heart and the tremendously thickened pericardium that is pulled aside. Stump of umbilical tape visible at base of pulmonary artery. Probe points to slight coarctation of aorta proximal to a 1 mm. ductus.

agitis and pancreatitis or an acute abdominal condition.

TREATMENT

Since the syndrome is a self limited condition of unknown origin and variable severity and duration, it is difficult to judge the effects of therapy. Nonspecific measures, designed to make the patient more comfortable while he recovers spontaneously, include rest in bed, the use of analgesics and antipyretics and pericardial or pleural taps if the patient's discomfort warrants these procedures. Five of thirty patients in whom the syndrome developed after open heart surgery received one or more thoracenteses, and three patients underwent pericardiocentesis as a therapeutic rather than a diagnostic measure. The fluid obtained was serosanguineous or straw-colored and was sterile on culture.

Antibiotics administered for the first postoperative week in the form of penicillin and Novobiocin®, with streptomycin in addition for the adults, had no apparent influence on the development of the syndrome. Neither did antibiotics appear to influence the course of the complication in the few cases in which the administration of these drugs was reinstituted or new ones utilized when the febrile illness appeared.

Steroids: Dresdale and his associates[9] in 1955 suggested the use of adrenal steroids as prophylactic and therapeutic anti-inflammatory agents in the syndrome in patients with rheumatic heart disease. Swan *et al.*[7] stated that patients with atrial septal defects with this syndrome responded rapidly to the administration of steroids.

We believe that the use of steroids should be restricted to those patients who are most severely

affected. Our experience with this agent is limited to four patients of the total of forty-five with the syndrome (included in this and the previous report). One of these patients, an extremely ill infant with multiple cardiac anomalies, died during the episode of pericardial reaction with tamponade and repeated pericardiocenteses. The other three had prompt symptomatic relief of pain, but the abnormalities in the electrocardiograms and roentgenograms did not disappear as rapidly.

Sequelae

One patient, referred to previously, died two weeks after operation with manifestations of the postpericardiotomy syndrome.

P. D. was operated on March 31, 1960, at the age of six months for banding of the pulmonary artery to relieve excessive pulmonary blood flow and hypertension. He had been treated for recurrent episodes of heart failure and pneumonia from the age of six weeks. Cardiac findings included a precordial systolic murmur and accentuated second sound in the pulmonic area. He was acyanotic. Roentgenograms showed enlargement of all four chambers of the heart and the main pulmonary artery. The lung fields were "flooded." Cardiac catheterization revealed an increase in oxygen content of 1.8 vol. per cent from venae cavae to right atrium and a further increase of 1 vol. per cent in the right ventricle, where the pressure was elevated to 67/2 mm. Hg. The catheter did not enter the pulmonary artery.

At operation an umbilical tape was tied around the main pulmonary artery until the pressure measured distal to the ligature was reduced by half. He improved slightly but on the sixth postoperative day pericardial tamponade developed. Pericardial taps that day and on the following day yielded 60 cc. of serosanguineous fluid. His condition improved temporarily following the removal of the fluid but the effusion reaccumulated. Prednisone was begun, and he required no more pericardiocenteses for the next five days. Nevertheless, his condition remained precarious and the chest roentgenograms indicated persistence or reaccumulation of pericardial fluid. On April 11, 1960, another tap, performed with electrocardiographic control as on previous occasions, yielded only small amounts of straw-colored fluid which appeared to be loculated. He died two weeks after surgery. All samples of fluid were reported sterile on culture.

At postmortem examination there was an intense pericardial reaction (Fig. 3). About 20 cc. of serous fluid was loculated in fibrinous pockets in the pericardial cavity, which was almost obliterated by dense, coarse adhesions. The entire pericardium was greatly thickened. Under the microscope, sections of pericardium showed fibrinous granulation tissue with intermixed and overlying fibrin strands.

Another patient with the syndrome died of another cause one month after operation and underwent necropsy. This forty-three year old woman, operated upon for aortic and mitral stenosis, manifested signs of the syndrome on the tenth through fifteenth postoperative days. She improved spontaneously and was ready to be discharged one month after the operation when she contracted Asian influenza and died of influenzal pneumonia. At necropsy the pericardial sac was obliterated by thick, fibrous adhesions.

The other patients recovered from the pericardial complication and, except for recurrences in a few, they have shown no signs of chronic effusion or of adhesive or constrictive pericarditis. To our knowledge, these late complications have not been reported following the postpericardiotomy syndrome, although pericardiectomy has been necessary in a few patients with a similar illness following hemopericardium due to trauma to the chest. For example, Goodkind, Bloomer and Goodyer[10] recently reported on two college students in whom recurrent pericardial effusions developed after nonpenetrating chest trauma. Adrenocortical steroid therapy appeared to control the effusions but pericardiectomy was deemed necessary in both for cure.

Etiology

The syndrome is more easily described than explained. We believe that it represents a delayed hypersensitivity phenomenon, most likely a reaction to blood, in a pericardial sac that has already experienced an immediate traumatic pericarditis following wide incision of the pericardium. The early traumatic pericarditis seems to occur uniformly in all patients in the first few hours after operation. We have obtained serial electrocardiograms on many of the patients in the operating room and in the first few hours postoperatively in the recovery room, as well as on successive days in the early postoperative period. Beginning in the first four to six hours after surgery they exhibited the serial electrocardiographic findings characteristic of acute pericarditis. It is usually not possible to listen for a friction rub because of the bandage covering the precordial region.

The few patients who have died in the first several hours after operation have demonstrated

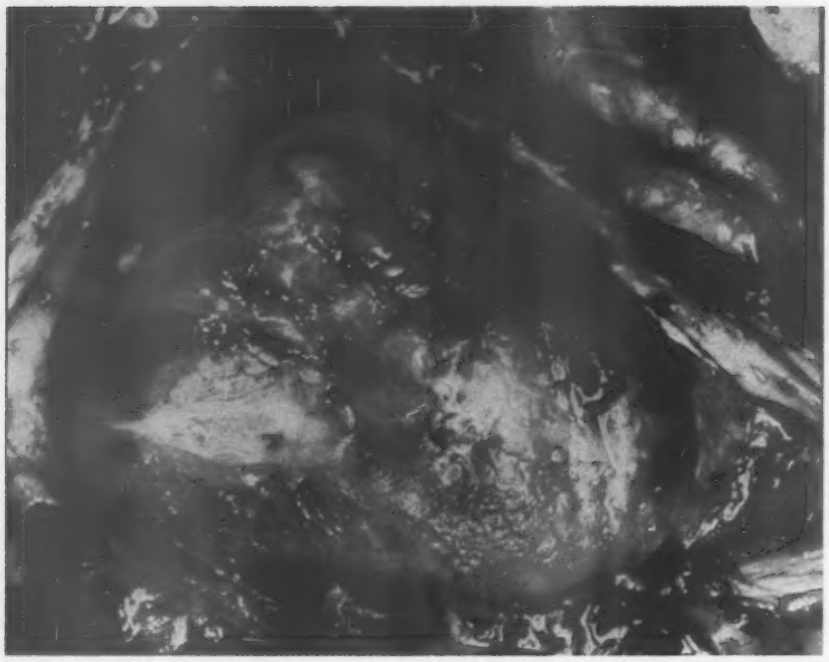


FIG. 4. P. B., five years of age. Tetralogy of Fallot. Death five hours after intracardiac repair. There is early traumatic pericarditis visible as granular markings and fibrin strands on surface of heart and pericardium that is laid back. Windows cut in lateral aspect of pericardium and spaces left for drainage between interrupted silk sutures were sealed by this pericardial reaction. Note blood clots within pericardium, especially overlying the closure of the right ventriculotomy. We believe the postpericardiotomy syndrome represents a hypersensitivity reaction, probably to blood, in a pericardium that has undergone a traumatic pericarditis like this.

at necropsy (Fig. 4) a granular appearance of the pericardium with early fibrin strands and with sealing off of the "windows" carefully left between stitches by the surgeons for drainage from the pericardial sac. Bloody fluid and sometimes clots of blood have been found within the pericardium. This early reaction we interpret as traumatic pericarditis.

The later reaction that is the postpericardiotomy syndrome occurs in only a portion of these patients, perhaps as a hypersensitivity reaction triggered initially in response to blood in the pericardial sac, with later recurrences brought on by less specific stimuli. The following patient illustrates well the initial traumatic pericarditis and the subsequent development of the postpericardiotomy syndrome four and three quarter months later with a recurrence quite similar to the first attack fifteen months after operation.

L. N., a nine and one-half year old colored girl, was operated upon on March 24, 1959, for an arteriovenous fistula between the right coronary artery and the right atrium. In the operating room the electrocardiogram showed no change in the form of the QRS group, S-T segments or T waves during a thirty minute period of trial occlusion before obliterating the abnormal communication by doubly ligating and transfixing the vessel near its point of origin. The thrill disappeared and the electrocardiogram remained unchanged as the pericardium was closed loosely with interrupted silk sutures and the operation completed.

Postoperative electrocardiograms showed changes characteristic of the development and evolution of acute pericarditis. The first electrocardiogram six hours after the operation showed minimal elevation of S-T segments in leads I and II. These changes were increasingly more marked twelve and twenty-four hours after surgery. On the second day the S-T segments remained elevated and the T waves in leads I and II flattened. On March 27, 1959, the S-T segments were isoelectric and T_2 and T_3 inverted. By the sixth postoperative day the form of the S-T segments and T waves returned to normal.

Drainage tubes were removed from the chest on the second postoperative day. She was afebrile after four days and antibiotics were discontinued on the sixth day. No murmurs or friction rub were heard when the chest bandage was removed. Teleoroentgenograms (Fig. 1A, B) showed a slight pericardial reaction and an area of infiltration or atelectasis in the right lung field when she was discharged, fully ambu-

latory on the fifteenth postoperative day. At home, she had no symptoms as she resumed full activity. She returned for follow-up examinations on April 22 and June 17, 1959.

The first episode of the postpericardiotomy syndrome occurred almost five months after the operation, on August 12, 1959. At 11:30 P.M. she awakened with a sudden pain under her left breast. It was more severe as she lay flat or took a deep breath. After twenty-four hours of intermittent precordial pain, she came to the hospital and was admitted. There was no antecedent illness or injury.

Examination showed temperature 38°C., pulse 130, respirations 44 and shallow, blood pressure 110/80 mm. Hg. She sat upright, alae flaring. The precordial area was tender to percussion, but no friction rub was detected and the heart sounds were heard well. Breath sounds were diminished over the right lower lung field. There was no venous distention, hepatomegaly or peripheral edema.

The white blood cell count was 16,000 with a normal differential count. Roentgenogram of the chest (Fig. 1C) revealed an increased cardiothoracic ratio and a distinct pericardial shadow outside the convexity of the main pulmonary artery. A pleural effusion was present on the left. The electrocardiogram showed elevation of the S-T segments and low amplitude of T waves in leads I, II and V_6. Other studies were unremarkable.

She stayed in bed and received neither antibiotics nor adrenal steroids. Over the course of the next week, electrocardiographic changes compatible with the further evolution and resolution of pericarditis occurred. Her temperature rose no higher than 38.4°C. and fell to normal on the fourth day, coincident with the disappearance of the precordial pain. The white blood cell count dropped to 7,000, and radiograms showed improvement (Fig. 1D).

When she became ambulatory after a week, the temperature rose over 38°C. again and the T waves in the electrocardiogram became inverted once more. Chest pain did not recur, however, and she was discharged on August 29, 1959, on modified activity at home. She had no complaints and the electrocardiogram was normal on two occasions during September 1959 and again in March 1960.

The second attack occurred fifteen months after surgery. Again there was no antecedent illness and the onset of left precordial pain was sudden as she was sitting in school on June 10, 1960. The pain radiated to the left shoulder and back; it was worse on inspiration and when lying down. When the pain was still present after five days, she was readmitted to the hospital.

The physical findings and the abnormalities on electrocardiogram and roentgenogram of the chest (Fig. 1E) duplicated those of the first attack, except for the absence of a pleural effusion.

Treatment consisted of rest in bed and the pain disappeared on June 20. While in the hospital, she had no fever. Tachycardia and tachypnea lasted only a few days. Daily electrocardiograms showed serial changes in S-T segments and T waves, indicative of pericardial reaction. By June 23 the tracing was normal again and the shadow on roentgenogram of distended pericardium had disappeared (Fig. 1F). She has experienced no recurrence of pain since discharge on July 11, 1960.

Similarities exist between the postpericardiotomy syndrome and that following myocardial infarction[11] or trauma to the chest.[10] A hypersensitivity reaction to blood in the pericardial sac may be the basic mechanism common to all three conditions. The syndrome also resembles idiopathic benign pericarditis, the etiologic basis of which may be viral but is still in doubt.

Summary and Conclusions

The postpericardiotomy syndrome occurred in thirty patients among 100 consecutive survivors of open heart surgery, utilizing the heart-lung machine, for repair of atrial and ventricular septal defects and the relief of pulmonic and aortic stenosis. Four patients experienced recurrences. Although an immediate traumatic pericarditis that can be demonstrated and followed by serial electrocardiograms develops in all patients undergoing wide incision and exploration of the pericardium, a delayed pericardial reaction, sometimes with pleural and pulmonary involvement, develops in approximately 30 per cent. This syndrome probably represents a hypersensitivity reaction to blood in a pericardial sac that has already undergone traumatic pericarditis.

Acknowledgment

We gratefully acknowledge the generous cooperation of Drs. Frank Glenn, George Holswade, Frank Redo and Edward Goldsmith who performed these operations. We are indebted to Drs. Peter Burkholder and Martin Cohen of the Department of Pathology for making available the kodachrome transparencies of Figures 3 and 4. Miss Ethel Longo and Mrs. Brack Hattler provided splendid assistance as senior electrocardiographic technician and as secretary.

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Postpericardiotomy Syndrome Following Traumatic Hemopericardium*

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IMPROVEMENTS in the emergency management of acute traumatic cardiac tamponade, both by pericardial aspiration[1–10] and by operative therapy,[11–18] have considerably lowered the mortality rate of patients suffering from traumatic heart disease. As a result, attention has been directed toward the more remote sequelae of traumatic hemopericardium, of which the late development of constrictive pericarditis[19–27] is important but fortunately rare.[7,10,14,29] A complication that is substantially more frequent and that adds greatly to the morbidity of traumatic heart disease is the development of recurrent pericardial and often pleural effusion, accompanied by chest pain, pyrexia and occasionally cardiac tamponade occurring weeks or months after the original injury. This complication has been known to surgeons for many years[4,7,9,20,30–37] but it has only recently commanded wider clinical interest because of its striking similarity[38–40] to such conditions as the postmyocardial infarction syndrome,[41] recurrent idiopathic pericarditis[42,43] and the postpericardiotomy syndrome that follows intracardiac surgery for rheumatic[44,45] and congenital[46,47] heart disease.

Some degree of controversy concerning the etiology of the postcommissurotomy syndrome still exists,[48–51] and views as to its pathogenesis and that of the postmyocardial infarction syndrome and recurrent pericarditis are purely speculative.[52–54] The presence of blood in the pericardial sac is a feature common to traumatic hemopericardium and the surgical postpericardiotomy syndrome, and a hemorrhagic pericardial reaction is seen in a significant number of cases of postmyocardial infarction syndrome[41,55] and idiopathic pericarditis.[56] Furthermore, the intrapericardial injection of autogenous blood and lipid fractions in dogs frequently produces an intense and prolonged inflammatory reaction.[22] Therefore, in order to define more clearly the pattern of events resulting from the presence of blood in the pericardial cavity of previously healthy subjects, the following investigation was undertaken.

CLINICAL MATERIAL

The hospital records of fifty survivors of traumatic hemopericardium seen at the Johns Hopkins Hospital over a twenty-two year period (1937 to 1959) were analyzed with particular reference to late manifestations of pericarditis. Trauma had resulted from penetrating stab wounds in forty-four cases, gunshot wounds in five and a fall in one instance. The diagnosis of hemopericardium was established either by aspiration or thoracotomy in forty-one cases. In the remainder it was assumed by virtue of the coincidence of chest trauma preceding clinical, radiologic or electrocardiographic signs of pericarditis. Criteria for "pericardial activity" were taken as the presence of an enlarged cardiac silhouette in combination with either pyrexia, a pericardial friction rub or chest pain of pericardial type.

RESULTS

GROUP I

The cases fell into three groups (Table 1). Thirty-four patients (68 per cent) were free of all signs of pericardial activity within fourteen days, the majority within eight days. Enlargement of the heart shadow, pericardial friction rub, pleural effusion and intermittent pyrexia were prominent features of the first hospital week. In four cases convalescence was prolonged because of acute renal failure (case reported by Stafford[57]) pneumonia, hemopneumothorax and wound abscess. The average duration of pyrexia (excluding these four cases) was six days, and temperature elevations be-

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TABLE I
Fifty Survivors of Traumatic Hemopericardium

Number		Pericardial Activity in Days
Group I	34 (68%)	2–14
Group II	5 (10%)	16–22
Group III	11 (22%)	40–208

tween 101° and 104°F. were frequently observed on the second to the fourth day. Leukocytosis occurred in almost half the patients and the degree of anemia was largely dependent on the extent of hemorrhage at the time of injury.

Electrocardiograms were recorded in twenty-seven cases. Single records taken in nine cases were interpreted as normal. S-T segment elevation and T wave changes characteristic of acute pericarditis were present in sixteen; transient atrial fibrillation occurred once and one record showed a pattern suggestive of inferior myocardial infarction.

Cardiac tamponade in varying degree was present in most patients, several of whom have previously been reported in detail.[1,3] The emergency treatment of these patients is indicated in Table II. Ten patients were subjected to thoracotomy. A wound involving the right ventricle was found in six, the right atrium in one and the left atrium in one. In two patients no cardiac laceration was found. Nineteen were treated by pericardial aspiration and the remaining five by supportive measures only.

Follow-up: Many of these patients have been followed for periods of two to twenty years. One patient died of pulmonary tuberculosis twelve years after his admission for hemopericardium. No thickening or scarring of the pericardium was noted at autopsy. There have been no known instances of constrictive pericarditis complicating this group.

GROUP II

A rapidly increasing pericardial effusion developed in five patients (10 per cent) during the second week of hospitalization at a time when convalescence appeared to be progressing without complication. Temperature elevation persisted for sixteen days in one patient, whereas in the remaining four it occurred as a secondary rise between the seventh and

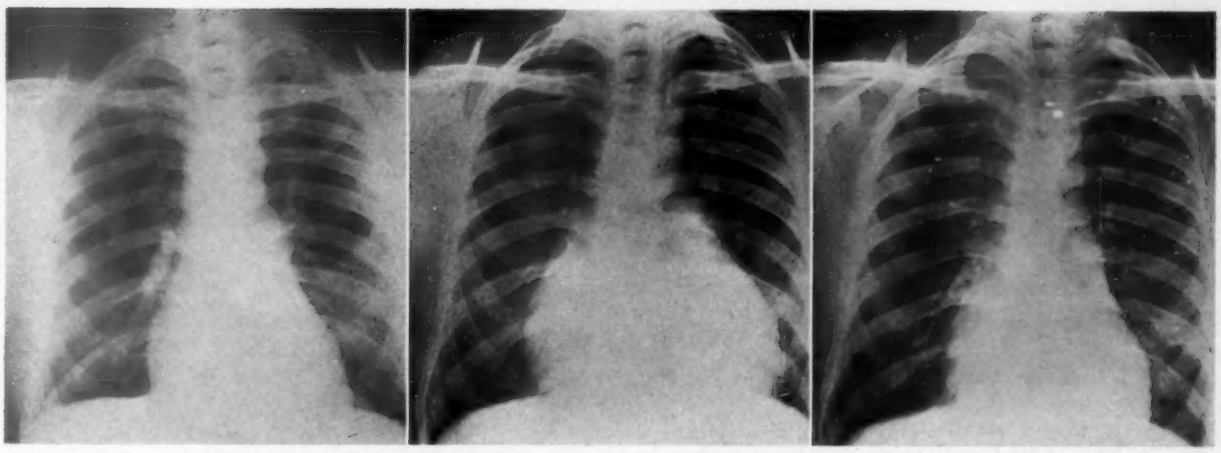
TABLE II
Emergency Treatment of Cardiac Tamponade

Trauma	Number	Aspiration	Surgery
Group I			
Stab	30	15	9
Gunshot	4	3	1
Group II			
Stab	5	2	3
Group III			
Stab	9	6	—
Gunshot	1	1	—
Blunt	1	—	—

twelfth day. A pericardial friction rub remained audible for twenty days in one patient. However, in all instances signs of pericardial activity had subsided by the end of the third hospital week.

Pericardiotomy was performed in three patients in this group (Table II) and large intrapericardial hematomas were evacuated. None had myocardial lacerations at the time of operation. In one patient, who was found to have a tear of the aorta with hemorrhage into the pericardium, transient acute renal failure developed in the postoperative period. Antibiotics were administered to all patients in the first week.

Illustrative Case: Delayed Pericardial Reaction with Rapid Spontaneous Improvement: W. H. (J.H.H. 382403), a negro man, aged forty-four years, was admitted on May 13, 1952, following stab wounds in the left chest, epigastrium and right lower abdominal quadrant. He was cold, clammy and pulseless but responded to supportive measures. Chest fluoroscopy showed a normal cardiac shadow and a moderate left hemothorax which was drained by means of a left chest catheter. An exploratory laparotomy revealed a laceration of the liver which was sutured. On the fourth postoperative day a chest roentgenogram was considered normal (Fig. 1A) and on the seventh day the patient was considerably improved. However, on the tenth day he complained of malaise and chest pain, and chest fluoroscopy showed an enlarged cardiac shadow with virtually absent pulsation of the cardiac borders (Fig. 1B). Pericardiocentesis yielded 65 ml. of sterile serosanguineous fluid but failed to influence the size of the cardiac silhouette. Several subsequent attempts at pericardial aspiration were unsuccessful. Temperature elevation had been present for the first two weeks, but on the sixteenth day the fever subsided and a chest radiograph taken on the twentieth day revealed a cardiac shadow of approximately normal size and contour (Fig. 1C).



A B C

FIG. 1. Serial roentgenograms of the chest in patient W. H. (Group I). A, fourth day after injury; B, tenth day; C, twentieth day.

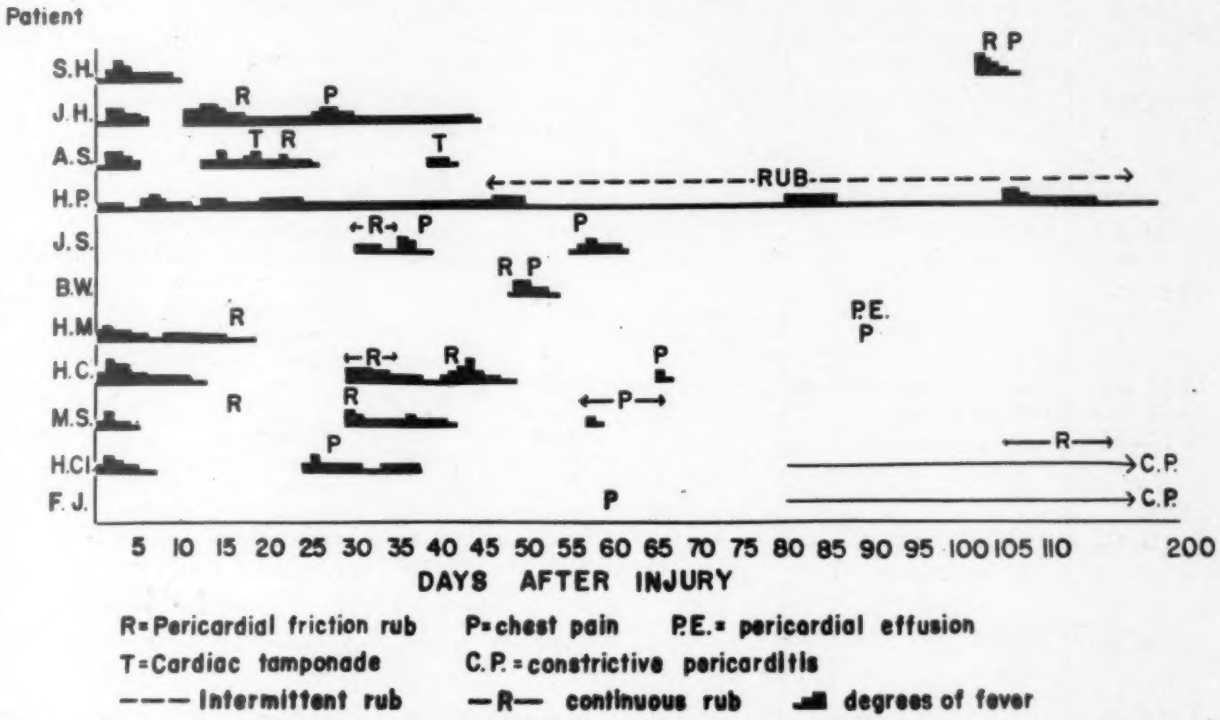


FIG. 2. Pyrexia in traumatic postpericardiotomy syndrome. Diagrammatic representation of the onset, duration and height of the pyrexia in eleven patients in Group III (see Table III).

GROUP III

In eleven patients (22 per cent) morbidity was prolonged for six to thirty weeks (Table I) by the development of recurrent attacks of pericarditis with effusion, pleural effusion, pyrexia and precordial pain. This complication has been designated the "traumatic" postpericardiotomy syndrome because of its close clinical resemblance to the "surgical" postpericardiotomy syndrome.

The group comprised ten males and one female with an age incidence of eighteen to sixty-one years. Nine stab wounds, one gunshot wound and one instance of nonpenetrating trauma constituted the modes of injury (Table III).

The major clinical features of the syndrome are depicted in Figure 2. *Pyrexia* was prominent in ten cases, both as a manifestation of the initial iliness and of the relapses. In one patient (Case 11, Table III) information regarding the early months of the illness was not available. Intermittent fever between 99° and 102°F. was common and occasionally spikes to 104°F. were observed in two patients. In others a

TABLE III
Pericardial and Pleural Effusions in Postpericardiotomy Syndrome

Case	Site of Injury	Pericardial Effusion			
		Day after Injury	Amount (ml.)		Characteristics
			X-ray	Aspiration	
1 (S. H.)	3 LICS	1, 6	Moderate	Failed	—
	5 LICS	103–105	Moderate	Failed	
2 (J. H.)	Left nipple	1	Moderate	70	Hemorrhagic
		18	Moderate	60	Grossly hemorrhagic Hematocrit 31 mm. (Venous blood 38 mm.)
3 (A. S.)	6 LICS	1	Moderate	150	Clotted blood ? venous
	Parasternal	11, 13	Marked	220, 200	Serosanguineous Sterile
		15, 19, 21	Marked	Failed	
		42	Massive	—	—
4 (H. P.)	2 LICS	1–202	Marked up to 208 days	Average 400	Hemorrhagic Hemoglobin 4 to 11 gm. per cent Total protein 5.4 gm. per cent White blood cells 4,700 Predominantly lymphocytic Sterile; guinea pig negative
5 (J. S.)	Right fractured ribs 7–10	30	Marked	—	—
6 (B. W.)	Left parasternal	54	Massive	Failed	—
7 (H. M.)	4 LICS	1	Slight	85	Hemorrhagic
		20	Marked	100	Altered blood Sterile
		86	Massive	—	—
8 (H. C.)	2 LICS	1	Moderate	45	Hemorrhagic
		43	Marked	Failed	—
9 (M. S.)	3 LICS	1	Moderate	300	Hemorrhagic
	6 RICS	57	Slight	—	—
10 (H. C.)*	Gunshot mid-sternum 5 ICS	1	Moderate	80	Hemorrhagic Hemoglobin 14 gm. per cent
		25	Marked	135	Hemorrhagic Hemoglobin 5.5 gm. per cent Sterile
11 (F. J.)†	6 LICS Parasternal	Inadequate information	—	—	—

* Pericardiectomy at eighteen months.
† Severe substernal pain at two months; died after pericardiectomy four years later.
LICS and RICS = left or right intercostal space.
LPE and RPE = left or right pleural exudate.
RLL = right lower lobe.

continuous low grade fever persisted for several weeks. The duration of pyrexia in the initial illness differed very little from that noted in Group I cases. Recurrences tended to be self limited and were often shorter and less severe with each successive relapse.

Substernal chest pain occurred in all patients. It was generally characteristic of pleuroperi-

TABLE III *Continued*

Pleural Effusion			
Day after Injury	Amount (ml.)		Characteristics
	X-ray	Aspiration	
3	Moderate LPE	—	—
104	Moderate LPE	150	Serous; sterile White blood cells 19,000
	Slight RPE	—	Predominantly monocytic Total protein 5.4 gm. per cent
15	Marked LPE	1,400	Serosanguineous Sterile Hematocrit—6 mm.
26	Marked LPE	—	—
	Marked RPE	1,020	Serosanguineous Sterile
33	Moderate LPE	900	Serous; sterile
	Moderate RPE	—	—
3	Slight LPE	—	—
42	None	—	—
3	Minimal left pleural reaction Pulmonary tuberculosis	—	—
30	Slight bilateral effusions	—	—
54	None	—	—
1	Moderate LPE	130	Hemorrhagic
89	None	—	—
1	Moderate LPE	—	—
45	Marked LPE	550	Serosanguineous Sterile Predominantly monocytic
5	Slight LPE	—	—
57	Pneumonitis RLL	—	—
2	LPE	650	Hemorrhagic
25	Slight bilateral effusions	—	—
±6 months	LPE	Frequent aspiration	? Serous

cardial pain, being sharp in quality, aggravated by breathing and movement and relieved by leaning forward. One patient picturesquely described a sensation "like a paper bag being blown up and down in my chest." Patient 11 developed severe substernal pain two months after injury and was treated as a case of myocardial infarction, without anticoagulants. Pain

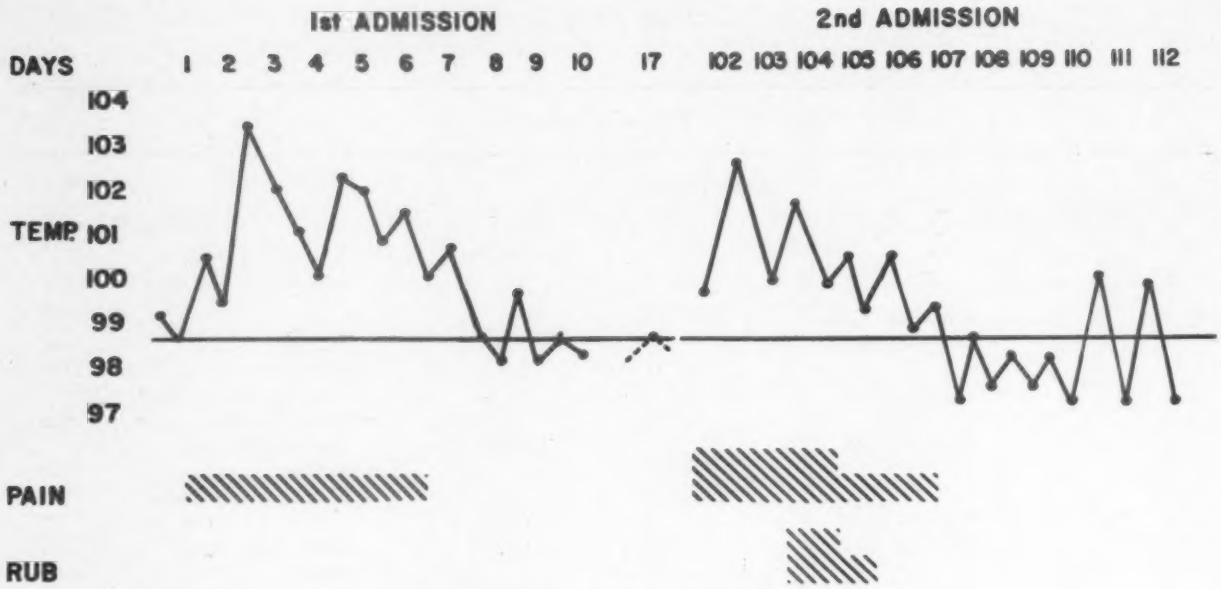


FIG. 3. Case 1. Temperature chart.

and pyrexia occurred concurrently in most instances. In two patients pain persisted for several months after all other signs of pericardial activity had disappeared.

Pericardial friction rub was recorded as a delayed sign in seven patients. It was more closely associated with pyrexia than with pain. In some patients it was mild in intensity and transient, whereas in two it persisted for several weeks.

Cardiac tamponade, with distended neck veins, hepatomegaly, ascites and edema, occurred late in the course of the disease in three patients. One of these (Case 3) recovered spontaneously and two patients developed constrictive pericarditis which required decortication at eighteen months and four years after the injury. These cases (Cases 10 and 11) have been reported in detail by McKusick, Kay and Isaacs.[25]

Table III presents the amount and nature of the *pericardial and pleural effusions* in each patient. A late pericardial effusion was documented either by roentgenography or aspiration in ten patients. It was hemorrhagic in many instances and serosanguineous in one. Cultures and guinea pig inoculations were consistently negative. The amount of aspirate varied considerably and in some cases large quantities were obtained. A noteworthy feature in four patients was a failure to aspirate fluid at a time when marked "cardiomegaly" was present radiologically.

Six patients developed pleural effusions at the time of relapse. These were bilateral in four and were generally small on the side opposite the site of injury. However, in one patient (Case 2) a marked right sided pleural effusion developed three weeks after a stab wound in the region of the left nipple. Over a liter of serosanguineous fluid was aspirated from the right pleural cavity on the twenty-sixth day. In the remaining patients the pleural fluid was either serous or serosanguineous, and predominantly monocytic in two.

The electrocardiogram was abnormal in all cases. Eight patients demonstrated S-T segment elevation at the time of injury. During the relapses slight segment elevation was evident in only two patients, but most cases showed widespread T wave inversion. These abnormalities often remained after other manifestations of pericarditis had subsided.

Hematologic studies during recurrences revealed a mild to moderate normocytic anemia (hematocrit range 24 to 37 mm.) in six, a neutrophil leukocytosis (up to 24,000) in five and a consistently elevated erythrocyte sedimentation rate.

Serum protein determinations were available in four patients. Two showed elevated total protein levels (8.2 gm. per cent with 3.4 gm. per cent globulin; and 7.9 gm. per cent with 3.4 gm. per cent globulin) while two were normal.

Treatment at the time of injury was nonoperative in all cases. Aspiration of the pericardium was successful in seven and failed in two. None had open pericardiotomy (Table II).

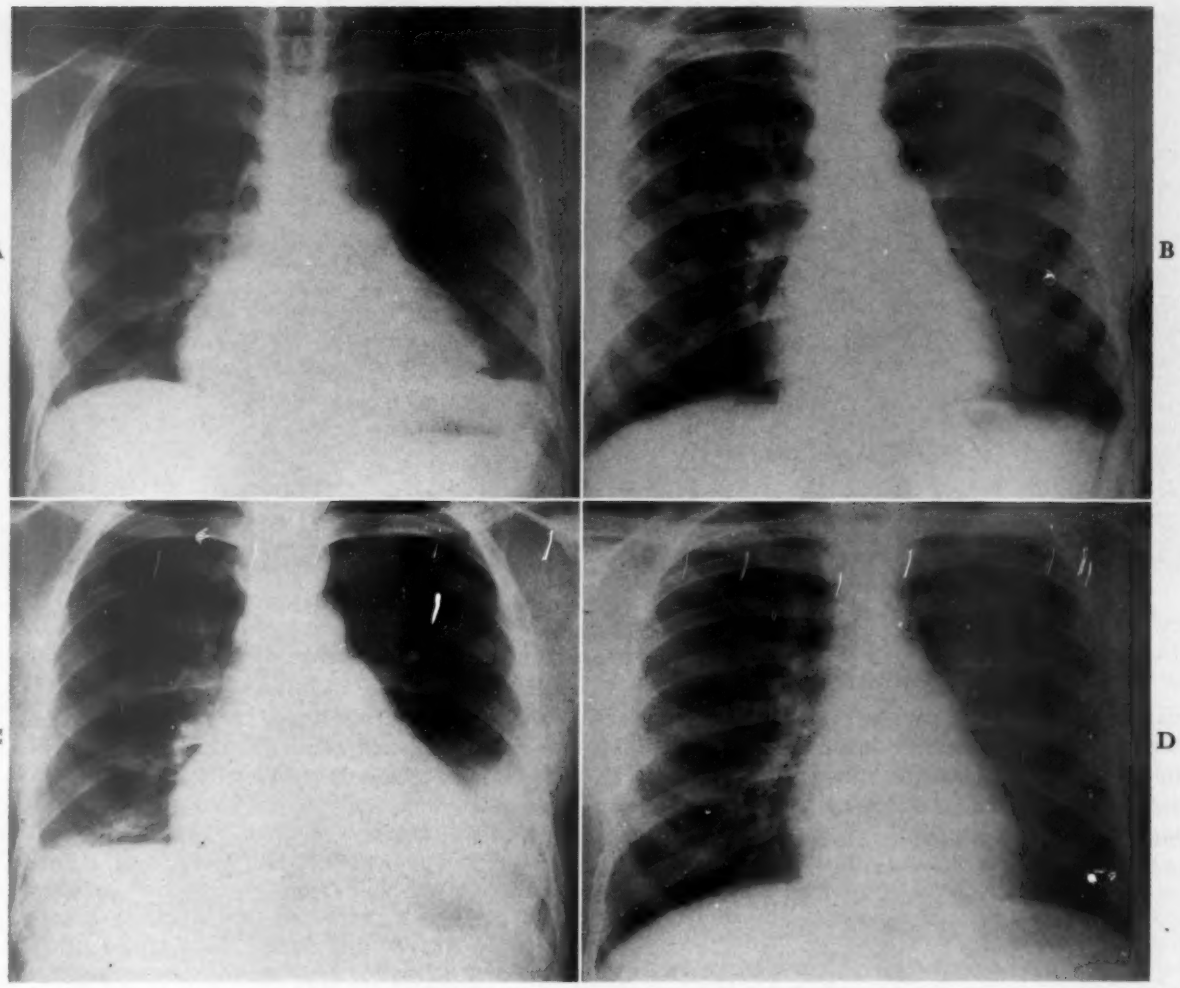


FIG. 4. Case 1. Serial roentgenograms of the chest. A, fourth day after injury, showing enlargement of the cardiac silhouette and a small left pleural effusion; B, seventeenth day, showing reduction in cardiac size; C, one hundred fourth day; note increase in cardiac silhouette and small bilateral pleural effusions; D, one hundred twelfth day; return to normal.

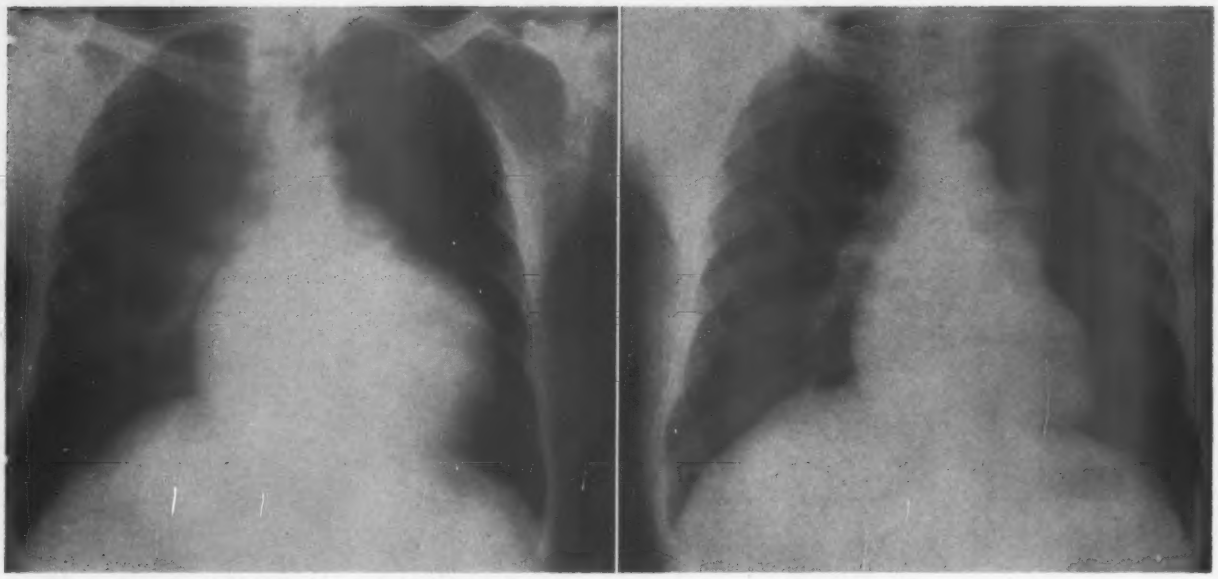
Short courses of antibiotics were administered in most instances at some time during the illness. However, relapses and remissions often occurred independent of antibiotic therapy.

Long Term Follow-up: Seven patients have been available for re-examination two to ten years after injury. One has cardiac enlargement attributable to hypertensive cardiovascular disease. Another has a "full-sized" heart, slight bilateral pleural thickening and a moderate reduction in his vital capacity. However, he has no clinical or electrocardiographic evidence of chronic pericarditis. Three patients have been victims of repeated assaults and injuries but have sustained no further damage to the pericardium.

ILLUSTRATIVE CASES

Case 1. Postpericardiotomy Syndrome with Bilateral Pleural Effusion: In S. H. (J.H.H. 531043), a negro male, aged thirty-two years, a hemopericardium and left pleural effusion developed following two stab wounds in the left parasternal region. His temperature ranged between 100° and 103.2°F. for the first six days, returning to normal by the tenth day (Fig. 3). An electrocardiogram showed striking S-T segment elevation in leads I, II, V_3 and V_5. A roentgenogram of the chest taken on the fourth hospital day showed moderate enlargement of the cardiac shadow and a left pleural effusion (Fig. 4A). He was discharged on the tenth day and on the seventeenth day the heart shadow was reduced in size (Fig. 4B).

He remained well until three months later when he presented with severe retrosternal chest pain and fever. A pericardial friction rub was first heard on the 104th day after injury. The cardiac silhouette was again enlarged and he now had small bilateral pleural effusions (Fig. 4C). Intermittent pyrexia was accompanied by leukocytosis and mild anemia. Repeated attempts to aspirate the pericardium were



A B

FIG. 5. Case 3. Serial roentgenograms of the chest. A, six weeks after injury; the patient showed signs of severe cardiac tamponade; B, one week after A; note reduction in heart size after single injection of Thiomerin.

unsuccessful, but 150 ml. of sterile straw-colored exudate, containing mainly mononuclear cells, was withdrawn from the left pleural cavity. A left sided pleural punch biopsy revealed nonspecific scar tissue only.

Amphenicol was administered for seven days. On the 112th day after injury he was asymptomatic and the roentgenographic appearances had returned to normal (Fig. 4D).

Case 3. Delayed Onset of Cardiac Tamponade with Spontaneous Resolution: A. S. (J.H.H. 176129), a negro male, aged fifty-four years was kept under observation for five days following a stab wound in the left chest. At the time of admission he showed electrocardiographic evidence of acute pericarditis. However, the cardiac shadow was only slightly enlarged and the venous pressure was normal. Pericardial aspiration yielded 150 ml. of venous blood.

On the eleventh day after injury he was readmitted because of chest pain and increasing dyspnea. On examination he was found to have cardiac enlargement, hepatomegaly, ascites and edema. Venous pressure was 400 mm. H_2O. Pyrexia, anemia and leukocytosis were present. Approximately 200 ml. of serosanguineous fluid was withdrawn from the pericardial cavity on two occasions, but subsequent attempts at aspiration were unsuccessful. He responded well to a diuretic regimen and was discharged five weeks after injury. At this time the heart shadow was still enlarged. An angiocardiogram confirmed that the enlargement was due to an increase in the size of the pericardial sac.

Six weeks after injury he presented once more with chest pain, pyrexia, severe cardiac tamponade and an enlarged cardiac silhouette (Fig. 5A). While his physicians were considering the possibility of pericardiectomy, he responded dramatically to a single injection of mercaptomerin (Thiomerin®) (Fig. 5B) and has subsequently remained well.

Case 4. Prolonged Pericardial Reaction in a Patient with Pulmonary Tuberculosis: H. P. (J.H.H. 344080), a negro male, aged twenty-four years, was admitted with signs of cardiac tamponade following multiple stab wounds of the chest. He responded well to pericardial aspiration. A roentgenogram of the chest revealed bilateral apical infiltration suggestive of pulmonary tuberculosis. This diagnosis was confirmed by sputum culture.

On the thirteenth hospital day chest pain developed and a sudden rapid increase in the size of the cardiac shadow. Signs of an active pericarditis, manifested by a continuous low grade fever, pericardial friction rub and frequent alterations in the size of the heart silhouette persisted for thirty weeks. In addition to the friction rub, a basilar diastolic murmur, which may also have been a result of the trauma, was audible. In spite of these findings, however, he complained very little and did not appear ill. Large amounts of intensely hemorrhagic fluid were aspirated from the pericardial cavity on numerous occasions. Acid-fast organisms were never recovered from this fluid.

He was treated with dihydrostreptomycin from the eleventh to the nineteenth week. The smouldering pyrexia continued and during this period he had one exacerbation of his illness, with accentuation of the friction rub, rise in temperature to 101.8°F. and further cardiac enlargement.

After cessation of antituberculous therapy the low-grade fever persisted for almost three months. Pericardiocentesis continued to yield large amounts of

FIG. 6. Case 4. Roentgenogram of the chest taken six months after injury. Fluid in the pericardial cavity has been partially replaced with air. Note the thin pericardium and the tuberculous infiltration in the right upper lobe.

hemorrhagic exudate. However, the pericardium remained thin throughout the illness (Fig. 6). For no apparent reason the pyrexia subsided during the twenty-eighth week after the injury and a roentgenogram of the chest taken on the 213th day showed a remarkable diminution in heart size.

On re-examination ten years later he was found to be asymptomatic. There was no clinical or radiologic cardiomegaly although the basilar diastolic murmur was still present.

Comment: Throughout this patient's long illness there were strongly conflicting views as to the etiology of the pericarditis. He has been cited on several occasions in the literature[25,58–60] as a possible example of tuberculous pericarditis caused by rupture of tuberculous lymph nodes into the pericardium as a result of trauma. We believe that his illness was entirely consistent with that observed in the traumatic postpericardiotomy syndrome.

COMMENTS

The potentially harmful effects of blood in the pericardial cavity were graphically described by Matas[61] fifty years ago. He believed that penetrating heart injuries invariably produced a hemorrhagic and serofibrinous exudate which led to inflammation, organization and extensive adhesion formation. He thus favored the view that blood should be removed from the pericardium as completely as possible. Sir Charles Ballance, in his celebrated Bradshaw Lecture[62] of 1919, summarily expressed the views of the times as follows: "The operation of paracentesis pericardii, or aspiration of the pericardium, should be, I think, banished from surgical practice."

Since that time attitudes have changed considerably, largely as a result of the demonstration by Blalock and Ravitch[1,3] that the nonoperative therapy of acute traumatic cardiac tamponade gives good results in the majority of cases. Nevertheless, argument concerning the relative merits of the two major forms of treatment continues.[8,16]

The present study shows that most individuals who survive the initial stages of the illness recover completely within a short period of time without overt signs of pericardial inflammation beyond the fourteenth day (Group I). Indeed, the absorption of intrapericardial blood progresses at a surprisingly rapid rate even in those patients in whom very little or no blood is removed by aspiration.

Recent studies on the absorptive capacity of serous membranes indicate the rate at which these hemorrhagic effusions may be removed. Thus Wilson and associates,[63] by injecting erythrocytes labeled with chromium[51] into the pleural cavity of animals, have demonstrated complete clearing of large hemothoraces within five or six days. Similar observations have been made with respect to the peritoneum.[64] Information concerning the rate of absorption of fluid from the pericardial cavity is limited.[65] However, there is no reason to believe that the healthy pericardium behaves differently from pleura or peritoneum although some evidence that absorption from the chronically inflamed pericardium occurs slowly has been presented.[66]

Five patients in the present series (Group II) showed delayed pericardial reactions with a slightly prolonged febrile response. This group is probably analogous in behavior to the milder examples of the postcommissurotomy syndrome, in which signs of activity are manifested by an accentuation and continuation of the normal postoperative sequelae.[45]

The analogy with the surgical postpericardiotomy syndromes, the postmyocardial infarction syndrome and recurrent idiopathic pericarditis is far more striking in the eleven patients who presented a relapsing and remittent febrile illness characterized by signs of pericardial and pleural inflammation (Group III). We have used the somewhat cumbersome term "trau-

matic" postpericardiotomy syndrome in preference to more elegant terminology in order to stress this analogy, since it seems likely that many of these syndromes have a common pathogenesis.

Recurrent pericardial effusion following cardiac injury is not uncommon.[30–40] It seems to be a special hazard in the presence of a foreign body[30–33,36] but may occur in its absence after both penetrating[39] and nonpenetrating chest injuries.[37,40] It might be anticipated that the widespread use of percutaneous left ventricular puncture as a catheterization procedure as well as the rising number of steering wheel injuries incurred in automobile accidents will lead to a greater incidence of this complication. Therefore, some of the more unusual features of the syndrome merit further comment.

RESPONSE TO THERAPY

Since the illness is self limited and the natural history so variable, the response to different therapeutic measures may be difficult to evaluate. Rapid alterations in heart size occur spontaneously and unpredictably. The dramatic improvement in signs of cardiac tamponade that may occur at a late stage of the disease without operative intervention is well exemplified by Case 3 (Fig. 5). Similar experiences have been recorded by others. Koucky and Milles[67] observed a patient in whom tamponade developed after a staphylococcal infection of a traumatic hemopericardium. At the seventh week after injury he had gross anasarca, but during the eighth week "without any treatment directed to the cardiac condition or the anasarca, a sudden dramatic change occurred" and the patient recovered. Abbott[34] cites a case with persistent tamponade four weeks after injury. While preparations were being made for decortication, a respiratory tract infection developed and surgery was deferred. Two weeks later he suddenly recovered without intervention. The improvement was attributed to the disappearance of an organized clot which could not be removed by aspiration.

Indications for Surgery: In patients submitted to operation for relief of cardiac tamponade in the early months after trauma the pericardium is generally edematous, thickened with inflammatory exudate and shows areas of granulation tissue in different phases of organization.[19,22,28,40] It is unusual to observe any persistent blood clot or appreciable amounts of liquid blood in the pericardial cavity,[28,40] a finding that might account for the difficulties encountered in aspirating the pericardium. The inflammatory reaction is potentially reversible at this stage. Hence it may be advisable not to submit patients with delayed signs of tamponade to thoracotomy until sufficient time has elapsed for spontaneous improvement to occur. Such a judgment may be extremely difficult; but on theoretic grounds it would seem reasonable to defer surgery until other signs of "pericardial activity," such as pyrexia, pain and friction rub, have subsided or the effects of steroid therapy have been observed. The excellent response to adrenocortical steroids in two patients with recurrent pericardial effusion following trauma to the chest[40] further emphasizes the similarity between the traumatic and the more familiar postpericardiotomy syndromes.[41,48]

ASSOCIATED PLEURAL EFFUSIONS

Another interesting feature of the traumatic postpericardiotomy syndrome is the development of bilateral pleural effusions following a unilateral injury, with involvement of the uninjured pleural surface.[39] Koucky and Milles[67] observed an encapsulated right sided pleural effusion in their patient who was stabbed in the left side of the chest. They suggested that the primary lesion in the pericardium became a focus from which bacterial or toxic inflammatory agents were disseminated to other serous membranes, resulting in a polyserositis which could involve the pleural or even peritoneal membranes. Valle[33] noted that in 80 per cent of patients who had a pericardial effusion after shrapnel wounds a left pleural effusion developed and in approximately 50 per cent a bilateral effusion developed. Reduction in the size of the pleural effusion was closely correlated with similar changes in the size of the pericardial effusion, and thoracentesis invariably yielded straw-colored serous fluid. He concluded that the pleural effusion results from compression of lung parenchyma by a large pericardial effusion.

In the present series a bilateral pleural effusion developed in four patients. In one patient (Case 2) who sustained a stab wound in the region of the left nipple, the cardiac silhouette had reduced in size at a time when a liter of serosanguineous fluid was aspirated from the right pleural cavity. We believe that this phenomenon is probably best explained as a spread of inflammatory exudate from the peri-

cardium to the opposite pleural surface by contiguity. However, the occurrence of bilateral and evanescent pleural effusions in the "surgical" postpericardiotomy syndrome[47] and the postmyocardial infarction syndrome[41] has been adduced as further evidence of a hypersensitivity reaction by some observers.[41,68]

RELATION TO INITIAL TREATMENT OF HEMOPERICARDIUM

The emergency treatment of traumatic hemopericardium may have some bearing on the subsequent development of the postpericardiotomy syndrome and constrictive pericarditis. Nonoperative measures were used in all patients in Group III in the present series (Table II). Reference to the literature shows that recurrent pericardial effusion occurs almost exclusively in those patients treated conservatively.[4,7,9,39,49] The cases reported by Samson[31] are an exception. However, he noted the occurrence of massive troublesome pericardial effusion in only those patients in whom the pericardium was tightly sutured at pericardiotomy. The complication was not observed when the pericardium was adequately drained into the pleural cavity.

The late development of constrictive pericarditis likewise occurs predominantly in patients treated nonoperatively.[19–28] Approximately thirty cases of post-traumatic constrictive pericarditis have now been compiled from the literature.[26–28] Most of these patients have shown signs of prolonged pericardial activity in the months following injury, so that the likelihood of permanent constrictive pericarditis complicating trauma is virtually limited to patients with the postpericardiotomy syndrome. Nevertheless, the over-all risk of constrictive pericarditis is small and might be lessened by steroid therapy in the active phase.[40] The incidence is thus not believed to be sufficiently high to contraindicate the use of nonoperative treatment in acute cardiac tamponade.

PATHOGENESIS

Infection: The pathogenesis of the "traumatic" postpericardiotomy syndrome is not well understood. It is unlikely that secondary bacterial infection of the hemopericardium can be incriminated since cultures of pericardial and pleural fluid have failed to isolate any pathogenic agent. Tuberculous pericarditis has been reported as a complication of trauma to the chest. However, neither the patient in the present series (Case 4) who had active pulmonary tuberculosis at the time of injury nor the frequently quoted case of White and Glendy[69] are convincing examples of such a process. The possibility that a latent virus infection is activated by injury to the myocardium cannot be entirely dismissed until further data are available. Such a mechanism has been postulated by Cohen, Dardick and Greenblatt[53] with respect to the postmyocardial infarction syndrome although subsequent studies by the same authors[58] have failed to substantiate this hypothesis.

Delayed Bleeding: Some observers have attributed the late onset of a hemorrhagic pericardial effusion to delayed hemorrhage from a wound of the myocardium.[70,71] Delayed massive hemorrhage is a well recognized[17,72] and often fatal[73,74] complication of cardiac wounds, which in proven cases has generally occurred in the first week after injury.[72,74] However, a slow continued leak into the pericardial cavity could produce a delayed hemopericardium without a necessarily fatal outcome.[70] Although such a process might have contributed to some of the cases in Group II of the present series, it seems unlikely that continued oozing would persist several months after injury particularly in cases in which pericardiocentesis fails repeatedly or operation reveals inflammatory exudate and no fresh blood.

Inflammatory Response to Blood: The pericarditis is best explained as a sterile inflammatory response of the intrathoracic serous membranes to the irritative effects of blood, blood clot and hemorrhagic pericardial fat pad. A superimposed accumulation of serous, serosanguineous and hemorrhagic exudate will lead to enlargement of the cardiac shadow, pyrexia and leukocytosis, and partial organization with scarring may produce cardiac compression.[35] At this stage the process is reversible in the majority of cases but exceptionally it may progress to chronic constrictive pericarditis.

A similar process probably occurs in the initial stages of the postpericardiotomy syndrome which follows intracardiac surgery. The development of recurrent pleuropericarditis following trauma in previously healthy subjects provides strong evidence against the rheumatic nature of the post commissurotomy syndrome.[44,58,61]

Similarity to Postmyocardial Infarction Syndrome: An intensely hemorrhagic pericardial exudate

may occur after acute myocardial infarction even in the absence of anticoagulant therapy.[41] It may be that the pericardial reaction which follows myocardial infarction is initially similar to that which results from trauma. However, the tendency to relapse, the striking response to adrenocortical steroids, the involvement of multiple serous surfaces and the finding of a lymphoid granulation tissue reaction in a fatal case of the postmyocardial infarction syndrome[41] have led to the theory that these syndromes are the result of an autoimmune reaction consequent to the release of cardiac antigen by necrotic myocardium.

In recent months the demonstration of circulating heart-specific autoantibodies in some cases of the postmyocardial infarction syndrome and the postcommissurotomy syndrome has provided some direct evidence for an autoimmunologic process.[68] However, these findings are difficult to interpret since the presence of antibodies may be the consequence rather than the cause of tissue injury.[68,75] In an experience limited to four patients with the postpericardiotomy syndrome following rheumatic heart surgery we have failed to demonstrate circulating antibody to nucleoprotein.[76] Furthermore, it appears that the "surgical" postpericardiotomy syndrome may occur even when no incision has been made into the myocardium.[46] In the present series it was not possible to determine whether the myocardium had been injured in the Group III patients, but three patients in Group II with the mild form of the syndrome had no demonstrable myocardial wound at operation. Indeed, it is not certain whether direct damage to the pericardium itself is essential for the development of the syndrome. Perkins and Elchos[77] have reported a patient with a stab wound of the aortic arch who had a mass of blood clot and hemorrhagic fat in the mediastinum at the time of operation. Although the pericardium was not opened, recurrent attacks of pericarditis developed with a sterile hemorrhagic effusion several months later.

Thus in our present state of knowledge it is difficult to account for the bizarre manifestations of these syndromes on the basis of an all embracing hypothesis.

Summary and Conclusions

1. An analysis of the hospital records of fifty survivors of traumatic hemopericardium seen at the Johns Hopkins Hospital over a twenty-two year period gave the following results: Sixty-eight per cent of patients recovered without sequelae within two weeks; in 10 per cent rapidly increasing pericardial effusions developed during the second week but the patients recovered by the end of the third week; and in 22 per cent recurrent pericardial and pleural effusions developed accompanied by pyrexia, precordial pain and occasionally cardiac tamponade. In the last group chronic constrictive pericarditis developed in two patients.

2. An analogy is drawn between the syndrome of recurrent pericardial effusion following injuries to the chest and the postpericardiotomy syndrome that occurs after intracardiac surgery. If the analogy is acceptable, the present study confirms the high incidence of the postpericardiotomy syndrome in nonrheumatic subjects and strongly supports the view that the postcommissurotomy syndrome results from surgical trauma and not from rheumatic reactivation.

3. Comparison is also made between the "traumatic" postpericardiotomy syndrome and the postmyocardial infarction syndrome. The potentially injurious effects of blood in the pericardial cavity are described and the possibility that hemopericardium may play an initiating role in the pathogenesis of the postmyocardial infarction syndrome is raised.

4. The relationship between the emergency treatment of acute cardiac tamponade and the subsequent development of recurrent pericardial effusion and constrictive pericarditis is discussed. It is concluded that although adequate drainage of the hemopericardium will prevent these complications, the incidence of constrictive pericarditis following trauma is not sufficiently high to contraindicate the use of nonoperative treatment in acute traumatic cardiac tamponade.

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Traumatic Pericarditis*

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The possibility of traumatic pericarditis is usually disregarded or given only slight consideration. The diagnosis often becomes submerged under the general classification of idiopathic pericarditis. This is noteworthy since experimentation with animals and clinical observation have shown it to be the most common of all nonpenetrating traumatic cardiopathies. The anatomic relations and characteristics of the pericardium, such as the attachment of the central tendons to the diaphragm, frequent fusion with the pericardial pleura, slight fixation by the sternal pericardial ligament to the inner side of the sternum, elasticity and irregularity of thickness, all make it vulnerable to injury.

In 1764 Mark Akenside[1] reported what is probably the first unquestionable case. A fourteen year old boy complained of chest pain, and a cough with hemoptysis developed immediately after he was struck between two ribs by the edge of a plate. Necropsy following his death six months and two days later revealed a totally adherent pericardium.

Method and Mechanisms of Injury

Before the automobile age the mechanisms of injury were, in order of frequency, falls from high places, blows from the fist or foot, heavy objects, wagon tongues and butting by animals. During the past forty years most blows to the chest have been caused by striking the steering wheel, instrument panel or back of an automobile seat. Those received on the anterior or left side of the chest most frequently produce pericardial injury. The force of the blows need not be sufficient to fracture the bony cage or cause more than minor contusion to the chest wall. The pericardium may also be injured by compression of the chest and the most frequent angle is from front to back. During violent compression, the great vessels are shut off, putting the fluid mass under great tension which produces rupture by expanding internal pressure. Tears at the roots of the great vessels appear to be due to violent displacement of the heart. In severe injuries caused by crushing or falling from a high place, the force is transmitted from within, rupturing the myocardium first, and then the visceral pericardium. Reiss et al.[2] observed areas of epicardial and pericardial hemorrhage with clinical evidence of pericardial damage, which was probably due to the frequent use of an electrocardiac pacemaker in a case of complete heart block with Stokes-Adams syndrome.

Pathology

The wound is usually produced by knives, bullets and fragments of bone; however, previously the instruments were spears and arrows. There are many important factors to be considered such as the character of the knife blade, whether sharp or blunt edge, pointed or round, narrow, thin, wide or thick; the caliber of the gun; character of the missile, whether more than one, lead or steel, soft or hard jacketed; the distance traveled and the angle at which it entered the body. The most frequent weapons used in modern times are knives, ice picks and pistols.

Blows varying in intensity from that of a hard rubber mallet to a 10-pound sledge hammer were struck on the chests of nineteen anesthetized dogs and the most frequent injury was to the pericardium.[3] There were pericardial and epicardial hemorrhages and tears and these lesions, when uncomplicated by myocardial contusion, were usually due to relatively moderate blows. In twenty-six human subjects who underwent necropsy as the result of severe extracardiac injury with only mild to moderate chest trauma, subpericardial hemorrhage oc-

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curred in all but two.[4] In the fourteen patients who died within two weeks, pericardial hemorrhage had occurred in ten and small pericardial or epicardial tears in four. In the twelve who lived from six to eighteen months, subpericardial fibrosis occurred nine times.

Subpericardial hemorrhages are usually anterior, near the large arteries and vary in size from small petechiae to large bruised areas. The infrequency with which these uncomplicated hemorrhages of the pericardium are found at necropsy is due to the tendency to recover.

Visceral pericardial tears are usually small slits which, together with small hemorrhages, lacerations and contusions, frequently heal without adhesions. In more extensive injuries, adhesion formation may vary from a single strand to an adhesive pericarditis with obliteration of the sac; however, small lacerations, hemorrhages and contusions of the pericardium frequently heal without adhesions. Infectious pericarditis, pneumopericardium, hemopericardium and herniation of the heart due to pericardial retraction are the most frequent complications of pericardial rupture. Myocardial rupture may produce a sharp, smooth, cleancut wound larger on the outside of the myocardium and pericardium than on the inside and usually does not approximate the place where the force was applied. As a rule, these lesions are lengthwise in the ventricles. Ruptures of the pericardium frequently occur at the base of the heart or margin of the auricles, and at the junction of the large vessels, especially the veins. These lesions are the result of violent displacement. The heart is occasionally torn completely loose and has been found free in the pleural cavity.

Case Reports

Case 1. A white man twenty-six years of age was involved in an automobile accident in which his car struck a utility pole and turned over. The patient arrived at the hospital unconscious and in shock. There was a small bruised area of the skin over the sternum probably caused by contact with the steering wheel which, however, was not broken or bent. Physical examination revealed the blood pressure to be 90/70 mm. Hg. Heart sounds were normal and the rate was 120 per minute. However, an occasional irregularity of the rhythm was noted. An electrocardiogram revealed this to be due to multiple ventricular premature contractions. Roentgenographic examination of the chest revealed the heart to be normal in size and contour and there were no fractures of the thoracic bony cage. The patient died in eighteen hours.

Autopsy showed a fractured skull as the cause of death. The heart and great vessels were found to be normal except for a small area of ecchymosis or bruising directly behind the sternum on the anterior surface of the heart. This area was 2 by 3 cm. in size and in the right ventricular wall just to the right of the anterior ventricular groove. There was a small tear measuring 1 cm. in length in the visceral pericardium just above the area of the myocardial and pericardial hemorrhage.

Case 2. A forty-four year old white man was caught by the clothing in a belt and pulley which threw him against the ceiling and then dropped him to the floor. Death was immediate. Autopsy revealed multiple fractures and contusions, but the most interesting finding was that the thoracic cage had been crushed laterally. This evidently was caused when the body was whipped against the ceiling which had only about 3 feet clearance from the pulley. There had evidently been violent displacement of the heart to the left. The entire thorax was full of blood and there was massive contusion of both lungs and tears in both right and left portions of the diaphragm. There was a large tear in the pericardial sac through which the apex of the heart had herniated. The inferior vena cava was completely torn free from the right auricle, and this tear extended up into the superior vena cava leaving only a small part of the right auricle intact.

Small puncture wounds of the heart show at first hemorrhage of the epicardium and myocardium with clot formation. Within five days, the clot is covered by a layer of cells and shortly afterward organization of the clot is accomplished and covered by epicardium. There may be abscess formation in the heart wall or pericardial sac. Aneurysm may form in the scar formation at the site of the injury and terminate in fatal rupture. The infrequency of wounds of the intrapericardial part of the aorta is due to its position behind the sternum.

If a *foreign body* enters the pericardial sac from the esophagus or the bronchi, there is invariably an adhesive pericarditis. There is always the possibility of abscess formation at the site of the foreign body, but usually it is encysted or encapsulated by fibrous tissue. Frequently there is some calcification and the fibrosis surrounding a bullet may even resemble a fibroma.

Clinical Features and Diagnosis

Pericardial Rupture or Tear: With rupture or tears of the pericardial sac, a double loud and soft systolic murmur with a sharp interruption is occasionally heard. This was described by

Morel-Lavallee[5] as similar to the sound of water striking the blade of a wheel. The sound may also resemble that produced by blowing into an empty bottle. Pericardial contusion and hemorrhage will produce a soft to rough systolic murmur which may be replaced at any time by a friction rub. These murmurs can disappear for a few pulsations or on change of body position.

Severe precordial pain developing immediately or at least within six to twelve hours is the most persistent symptom. Dyspnea and orthopnea occasionally occur and there may be precordial distress on breathing. Tenderness over the precordium and palpitation are symptoms which persist for some time. If the heart sounds appear distant at any time, a roentgenogram, electrocardiogram or even pericardial tap should be performed immediately to ascertain the possibility of a hemopericardium. In all cases, roentgenographic examination should be made as soon as possible. If this is performed early, the films can be compared with subsequent ones if a question arises in regard to cardiac aneurysm or hemopericardium. A roentgenokymogram or electrokymogram offers not only means of diagnosis but also the possibility of locating the lesion.

Cardiac Rupture: Cardiac rupture produces sudden collapse and chest pain. At first the heart rate may be slow but as tamponade develops, the pulse becomes rapid and weak. The heart sounds are muffled and distant, arterial pressure falls and venous pressure is increased with engorgement and distention of the neck veins. As the circulation fails, marked pallor with cyanosis develops and the patient finally becomes unconscious. Percussion will show an increase in the area of cardiac dullness and the diagnosis can finally be established by tapping the pericardial sac and withdrawing blood. It is also possible that pericardial as well as myocardial injury can occur to a heart that is already damaged by some other type of disease. Uncomplicated pericardial injury does not appear to cause cardiac arrhythmia; associated myocardial contusion appears to be necessary. The unipolar leads are useful in locating the position of injury and identifying traumatic pericarditis. The electrocardiographic changes are the same as in any type of pericarditis and frequently do not occur until after a period of twenty-four to forty-eight hours. Therefore, serial tracings should be taken. They are important also because the electrocardiogram tends to return to normal. In severe cases, the sound advice of Beck[6] is that repeated tapping of the pericardial sac should be performed not only to confirm the diagnosis but also to relieve cardiac tamponade until surgical intervention is possible. The most frequent late complications of wounds to the pericardium are adhesion, obliteration and calcification. Mediastinopericarditis has occurred in a few reported cases.

Penetrating Wound of Pericardium: The diagnosis of penetrating injury to the pericardium should not necessarily be difficult. A significant sign is a wound in the precordial region. However, the course of a bullet or knife thrust is notoriously misleading and it may be somewhat distant with copious hemorrhage. It is safer to explore the pericardium than to take the chance of an undiagnosed hemorrhage and cardiac tamponade. There is frequently a symptom-free period of from five to ten minutes following the injury, and usually by this time a cessation of bleeding from the external wound is noted. Loss of consciousness may be the result of an asystole due to the hemopericardium or cerebral anemia as the result of the marked hemorrhage. Occasionally, there is a raving delirium and frequently restlessness with muscular contractions and even convulsions. Probing is inadvisable but it is possible to determine whether the heart has been injured if the instrument pulsates. The external hemorrhage may be small or excessive, pulsating, oozing or a steady flow.

When a penetrating wound of the chest involves the pericardium, there is invariably severe shock with unconsciousness, cold perspiration, increased respiration, widely dilated pupils, with all other classic signs. The facial expressions indicate great distress and anxiety. Frequently there are signs of air hunger such as sighing, yawning and gasping for breath. The pulse is very weak and frequently imperceptible. If hemorrhage is into the pericardial sac, anemia is not as pronounced as when it occurs into the thorax. Cyanosis, when it occurs, depends upon the size of the wound, the amount of hemorrhage and interference with respiration. Venous pressure is frequently increased and neck veins are engorged. There is extreme dyspnea and marked anxiety. The arterial blood pressure drops and it may become unobtainable. Delirium following wounds to the heart and pericardium is probably due to prolonged cerebral anemia as

the result of extensive hemorrhage and low blood pressure.

Cardiac Tamponade: A large area of cardiac dullness would suggest the possibility of hemopericardium. The so-called "spinning wheel or mill sound" is rarely heard. The most precise information is obtained by roentgenographic examination which reveals the size and immobility of the cardiac shadow and the presence of a hemopericardium. It should be remembered, however, that death can occur from a rapidly developing tamponade which started from an amount of blood too small to change the contour of the cardiac silhouette. The diagnosis of cardiac tamponade is practically certain if there is a rising or high venous pressure and a falling or low arterial pressure with the absence of cardiac pulsations on fluoroscopic examination. Abnormal ballistocardiographic tracings may be somewhat helpful. If the diagnosis is otherwise impossible, aspiration should be performed.

Roentgenographic examination will also reveal the presence of constrictive adhesive pericarditis. When there is inflammation of the pericardium, pain is acute and cutting in character. Pain may be continuous or periodic and brought on or intensified by exertion or change of position. Dyspnea, another frequent symptom, is usually present only on exertion unless heart failure occurs. There are frequent attacks of palpitation and tachycardia. Premature contractions are probably the most frequent type of arrhythmia.

Foreign Bodies: Sometimes foreign bodies are small objects or are not of opaque material and therefore cannot be seen on roentgenographic examination. In order to ascertain whether a foreign body is intracardiac, the shadow should be seen under the fluoroscope, within the cardiac shadow in the anterior-posterior and both oblique positions, and when the body is flexed from right to left at the waist. It should also be synchronous in movement with the heart shadow and not the diaphragm. The history and symptoms may suggest the presence of a foreign body but the diagnosis is definitely established only by finding and locating the body by roentgenographic examination. It is very difficult and requires considerable knowledge and skill to state with assurance the location of a foreign body in or about the heart. With some patients, symptoms occur only when an attempt is made to resume an active normal life. The difference in the consequence depends on the position of the foreign body in the heart.

Treatment

Acute Injuries: Large doses of antibiotics should be given immediately and even injected directly into the pericardial sac in an attempt to prevent infectious pericarditis. However, if infection develops, it necessitates complete drainage, and if at all possible the patient should bend forward as though he were standing on his head. This maneuver will cause the ventricle to move forward and the cul-de-sac of Haller will be open. It is safer to perform exploratory pericardiotomy than to run the chance of death from cardiac tamponade or hemorrhage. Rather than try to separate the pericardial visceral layers in pericarditis, a large portion of the pericardium should be removed.

Foreign Bodies: In an old wound with a foreign body within the pericardium when the patient appears in perfect health with no functional disturbance, it is important to consider the psychic elements before definite statements are made. Frequent neurotic manifestations develop depending upon the attitude of the patient to the knowledge that he harbors a foreign body. This must be guarded against with psychotherapy, directed not only to the patient but also to the overanxious relatives and friends. Surgical intervention should be weighed very seriously since accumulated experience has shown that in time many and probably most foreign bodies become safely encysted and will do no harm. However, if the presence of a foreign body in the heart is found in the acute period following injury, removal may be desirable in order to prevent infection, myocardial rupture or other further complications. If definite symptoms develop or persist, intervention should be considered. A foreign body in the pericardium that is causing symptoms can be easily removed with little risk. Most surgeons advise the removal of long, thin objects such as needles and wires, and large foreign bodies in the pericardium probably should be removed as early as practical.

Prognosis

A number of cases have been reported in which foreign bodies within the pericardium have been tolerated for a long period of time. Cases have been reported in which soldiers

have returned to active duty and combat after removal of a foreign body, and others have engaged in athletic contests and hard labor.

The prognosis becomes grave if traumatic pericarditis is complicated by inflammation of the endocardium or myocardium, and death depends upon the size and speed of the hemorrhage. However, once the acute phase has passed, the prognosis for small pericardial and subpericardial lesions when healed uneventfully is good; but the more extensive or obliterating injuries may result in interference with cardiac output and hasten heart failure. Cardiac fixation due to adhesions frequently results in permanent disability. Cardiac tamponade frequently causes sudden death or rapid failure. The heart can also be embarrassed by clot formation in the pericardial sac from even a small wound or obliteration of the the sac by adhesions. This frequently results in pericardial calcification and an armored heart. A rupture of the pericardial sac allows blood to escape which prevents tamponade, and death is delayed. The prognosis for partial or even complete recovery in cases of uncomplicated mild and moderate cardiac injury is good. Uncomplicated hemorrhages have the best prognosis. The juvenile heart has a more favorable prognosis.

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Nontraumatic Hemopericardium

An Analysis of 105 Cases*

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HEMOPERICARDIUM is usually a sudden and massive catastrophe, giving rise to a rapidly fatal cardiac tamponade. Until recent years the diagnosis has usually been unsuspected during life, the lesion being little more than a pathologic curiosity. By far the most common nontraumatic cause of hemopericardium is rupture of a myocardial infarct, followed in frequency by rupture of an aortic aneurysm.

The development of surgical technics in the treatment of the underlying causative disease as well as the tamponade emphasizes the necessity for early diagnosis in order that appropriate therapy may be instituted.

There are a number of excellent articles on hemopericardium incidental to myocardial infarction[1–5] but reviews of the causes of hemopericardium are sparse. Reviews published by Comroe[6] and Fulton[7] stand out in this neglected field.

The present study is a review of cases of hemopericardium encountered at the Los Angeles County Hospital.

METHOD AND MATERIAL

One hundred five cases of nontraumatic hemopericardium were encountered among 21,000 consecutive autopsies performed at the Los Angeles County Hospital from January 1, 1947, to June 1, 1957. Cases were chosen in which the hemopericardium was considered to be a direct or contributing cause of death by the autopsy prosector. For inclusion in this series, the pericardial fluid must have resembled blood in appearance; instances in which the fluid was merely "blood-tinged" or "serosanguineous" were excluded.

RESULTS

A tabulation of the causes of hemopericardium and their frequency in the present study are shown in Table I. Hemopericardium was most frequently due to acute myocardial infarction which comprised sixty-three (60 per cent) of the total number of cases. Next in frequency were aneurysms of the aorta, comprising thirty-five (33 per cent) of the total. The majority (86 per cent) of aneurysms were of the dissecting type. Rupture of a syphilitic aneurysm occurred in four instances and rupture of a mycotic aneurysm involving a coronary artery in one instance. Four cases (4 per cent) were due to metastatic carcinoma; three (3 per cent) were the result of blood dyscrasias, including two with leukemia and one ill defined hemorrhagic diathesis in a newborn.

The amount of blood within the pericardial sac was recorded in eighty-nine of the 107 cases and varied in amount from less than 100 to 1,000 ml., although in most instances the amount was 500 ml. or less (Table II). Accumulations of over 500 ml. of blood were present in fourteen cases. The blood was usually clotted at the time of autopsy and occasionally formed a complete cast of the pericardial sac (Fig. 1).

MYOCARDIAL INFARCTION

Age and Sex: During the period of this study there were 1,443 instances of acute myocardial infarction encountered at autopsy, including sixty-three (4 per cent) with hemopericardium. There were more women (thirty-four) than men (twenty-nine). There was no significant age difference, the average age of men being seventy years, and of women sixty-eight years. The youngest age in each sex was fifty-two years for women and fifty-six for men. Comparison by decades revealed that the vast majority occurred in patients between the ages

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TABLE I
Causes of Hemopericardium in 21,000 Autopsies

Causes	No. of Cases
Acute myocardial infarction	63
Ruptured aneurysm	35
Dissecting aneurysm of aorta	30
Syphilitic aneurysm	4
Mycotic aneurysm of coronary artery	1
Neoplasm (metastatic carcinoma)	
Breast	2
Lung	1
Stomach	1
Blood dyscrasia	3
Leukemia	2
Hemorrhagic diathesis in newborn	1
Total	105

TABLE II
Volume of Pericardial Blood

Volume (cc.)	No. of Cases
0–100	9
0–100	9
101–200	20
201–300	20
301–400	16
401–500	10
501–600	4
601–700	1
701–800	5
801–900	2
901–1000	2
Total	89

of sixty and eighty years, with essentially the same distribution in the two sexes. With the exception of one Negro, all were Caucasians.

Time of Rupture: A preponderance of the cases of hemopericardium occurred early following myocardial infarction (Fig. 2), the largest number during the first twenty-four hours. Thereafter, the incidence decreased exponentially. The interval from time of onset to rupture was known in forty-two cases: thirty-four (81 per cent) occurred during the first week following infarction and only three (7 per cent) occurred after two weeks.

Hypertension: Approximately one-third of the patients either had hypertension (blood pressure, 150/100 mm. Hg or above) or had had hypertension. Cardiac hypertrophy was present in sixteen of thirty-eight instances in which the heart weight was recorded at autopsy. A history of prior myocardial infarction was

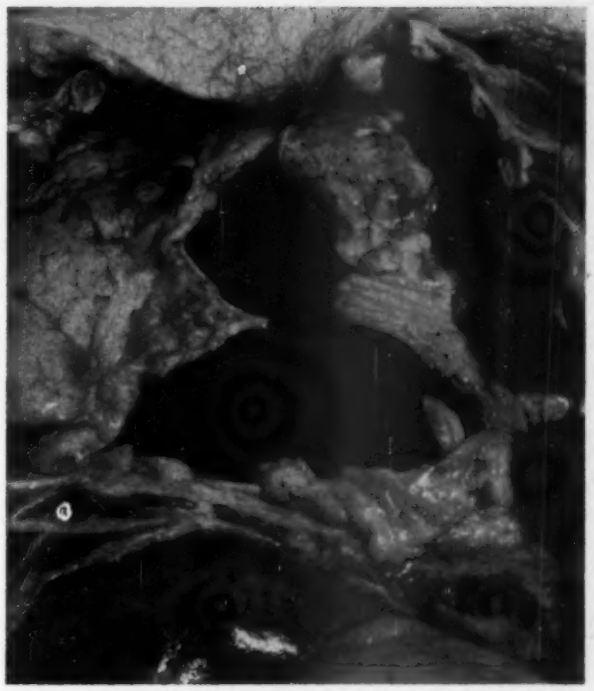

FIG. 1. Hemopericardium following myocardial infarction, with clotted blood forming a cast of the pericardial sac.

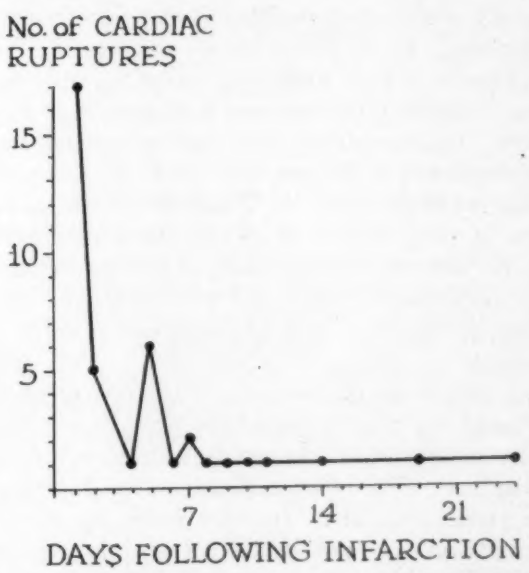

FIG. 2. Relation of cardiac rupture to survival time following infarction.

seldom present, only four such cases being encountered.

Anticoagulant Therapy: Fifteen patients with hemopericardium due to myocardial infarction were receiving anticoagulants (heparin or dicumarol) during their hospital stay. In neither of the two instances of pericardial hemorrhage in which a careful search failed to reveal a site of perforation had anticoagulants been adminis-

TABLE III
Site of Perforation of Ventricle Following Infarction

Sites	No. of Patients
Left ventricle	55
Anterior	32
Apex	18
Midportion	7
Base	3
Not recorded	4
Posterior	15
Apex	3
Midportion	4
Base	3
Not recorded	5
Lateral	8
Right ventricle	2
Posterior	1
Apex	1
Perforation, site not recorded	4
No perforation found	2

tered. Hemopericardium was suspected clinically in three patients. In each the sudden onset of gasping respirations, cyanosis and shock rapidly progressing to death led to the correct diagnosis. In fourteen cases myocardial infarction was not suspected prior to autopsy; nine of these patients were belligerent or confused; the remaining five had symptoms suggestive of other diseases.

Sites of Perforation: In Table III are shown the sites of perforation of myocardial infarcts in the present study. In most instances perforation occurred through the left ventricle. Anterior perforation was approximately twice as frequent as posterior perforation. The apex of the heart was the site most frequently involved followed by the mid-portion and base. Posterior perforations had no predilection for site of rupture. Two perforations occurred through the right ventricle. In four cases the site of perforation was not described and in two no perforation was found.

ANEURYSMS

Site of Aortic Dissection: Hemopericardium was the cause of death in thirty (47 per cent) of a total of sixty-three cases of dissecting aneurysm of the aorta. In these cases dissection involved the ascending aorta. In twelve dissection was limited to this segment of the aorta; in four dissection extended to some portion of the arch; two involved some portion of the descending thoracic aorta; the entire thoracic aorta was involved in ten; and in two the extent of dissection was not mentioned. In contrast, of thirty-three cases of dissecting aneurysm without hemopericardium encountered during the period of this study, only nine (27 per cent) had dissection of the ascending aorta while twenty-four (73 per cent) had dissection limited to the arch, descending or abdominal aorta.

The majority or 76 per cent of patients with dissecting aneurysm with hemopericardium had intimal tears located in the ascending aorta, whereas only 10 per cent of patients with dissections without hemopericardium had tears at this site. The majority (64 per cent) of patients with dissections without hemopericardium had intimal tears in the arch of the aorta or beyond, the most frequent site being the aortic isthmus.

In only one case of dissecting aneurysm with hemopericardium was the pericardial hemorrhage suspected prior to death. This case is briefly summarized as follows:

Aortic Dissection with Hemopericardium: A fifty-three year old man was admitted to the hospital on August 6, 1956, complaining of sudden onset of severe substernal pain which was referred to the shoulders, neck, anterior chest and legs. He was sweating profusely. The brachial blood pressure was 110/50 mm. Hg (right) and 150/ 70 mm. Hg (left). The left radial arterial pulse was felt earlier and stronger than the right. A thrill was palpable over the left carotid artery, and a thrill and murmur over the right carotid artery Rales were present in the bases of both lungs. Heart sounds were almost inaudible; no murmurs were found. A diagnosis of dissecting aneurysm of the aorta was made. Three and a half days after the onset of symptoms the pain suddenly increased. An intern was called who observed distended neck veins and an increase in the area of cardiac dullness and suspected the development of hemopericardium. The patient died a few minutes later.

At autopsy the pericardial sac was filled with blood. Dissection involved the entire aorta and extended into the three major branches arising from the aortic arch. A transverse tear measuring 3.5 cm. was present 3 cm. above the aortic valve.

Ruptured Aneurysm: Hemopericardium was due to rupture of syphilitic aneurysms in four cases. In each a saccular aneurysm was present in the ascending aorta and varied in size from 5 to 11 cm. in diameter. Each had ruptured into the pericardial sac. In one instance a sinus tract extended downward for a distance of 6 cm. from the aneurysm to the pericardial sac.

NEOPLASM

Pericardial hemorrhage was the result of metastatic carcinoma in four cases including one of bronchial origin, two from the breast and one arising in the stomach. In the bronchogenic carcinoma metastases to the pericardium were apparently the result of direct extension from an adjacent focus in the lung. All the tumors had widespread metastases, at least five or more sites in addition to involvement of the pericardium. In none of the four did the pericardial fluid contain clots. The amount of fluid varied from 250 to 600 ml. with an average of 400 ml.

BLOOD DYSCRASIAS

Hemopericardium was the result of a blood dyscrasia in three instances. Two occurred in leukemia including acute monocytic leukemia in a sixty-nine year old man, and acute myelogenous leukemia in an eleven year old boy. In the latter instance sternal puncture had been performed shortly before death, blood had diffused into the retrosternal tissues and a hemorrhagic area was present on the anterior surface of the right ventricle directly under the course of the sternal needle. Although perforation of the sternum during marrow aspiration no doubt contributed to the hemopericardium, the presence of an underlying hemorrhagic diathesis was indicated by the presence of numerous petachiae in the skin and a moderate amount of subdural hemorrhage. In the third case hemopericardium was the result of hemorrhagic diathesis of unknown origin, occurring in a twenty-day old male infant who was born prematurely.

TRAUMATIC HEMOPERICARDIUM

Only two cases of hemopericardium had to be excluded from the present series because of traumatic origin. The infrequency of traumatic hemopericardium is no doubt related to the fact that such cases become coroner's cases, and their protocols are not part of the records at this hospital. Of the two one followed an automobile accident; the other was an accidental perforation of the right ventricle by a catheter used for intravenous infusion. The latter case, because of its rarity, is summarized as follows:

Perforation of Right Ventricle by Polyethylene Catheter: A sixty-three year old white woman was admitted to the hospital having had lethargy and mental confusion for twelve days. A diagnosis of chronic alcoholism and cirrhosis of the liver was made. Fifteen days after admission a polyethylene catheter 60 cm. long was inserted into the median basilic vein of the left arm for purposes of intravenous infusion. She complained of mild distress in the chest immediately after insertion of the catheter, became apprehensive and died thirty-six hours later.

FIG. 3. Ecchymosis at apex of right ventricle due to perforation by catheter.

At autopsy the pericardial sac was bulging with 500 ml. of blood. The heart was small; a perforation 1 ml. in diameter was found over the anterior portion of the apex of the right ventricle, extending through an area of normal myocardium (Fig. 3). In this case a polyethylene catheter inserted for intravenous infusion perforated the apex of the right ventricle. Leakage was gradual, the patient surviving perforation by thirty-six hours.

COMMENTS

In most cases in the present study hemopericardium was sudden in onset and massive in amount, giving rise to a rapidly fatal cardiac tamponade. Thus in only four of the 105 cases was a correct clinical diagnosis made, based on the recognition of the typical symptoms and signs of pericardial effusion.

In the present study, as in other series, the patients with myocardial infarction terminating in cardiac rupture were elderly; no patient was below the age of fifty years. A slight preponderance in women was noted, a finding also

present in the earlier studies of cardiac rupture in this same hospital by Edmondson and Hoxie[1] and Oblath et al.[2]

Nine of the sixty-three (14 per cent) patients with myocardial infarction and hemopericardium were confused, irrational or belligerent during their hospital stay. The lack of cooperation and frequently associated physical hyperactivity may account for the frequency of cardiac rupture in these patients. A high incidence of rupture following acute myocardial infarction was noted by Jetter and White in mental patients.[3] The tendency for rupture of the heart to occur early, especially in the first eight days following the onset of infarction, is confirmed.[4]

Aarseth and Lange[5] have observed that rupture is one and a half to two times more frequent in patients receiving anticoagulants than in control patients. They encountered five cases of hemopericardium without cardiac rupture in the group who were treated but none in the control group. We encountered only two patients with hemopericardium without rupture, neither of whom received anticoagulants.

Hemopericardium is a complication of dissecting aneurysm involving the ascending aorta and seldom occurs with dissecting aneurysm beginning in the descending thoracic aorta. In instances of dissecting aneurysm with hemopericardium, intimal tears are generally present in the ascending aorta; those patients without hemopericardium usually have intimal tears in more distal sites.

Nontraumatic causes of hemopericardium not encountered in this study include tuberculosis,[8,9] uremia,[10,11] bacterial endocarditis or myocardial abscess,[12] periarteritis nodosa,[13] primary tumors of the heart[14,15] and nonspecific pericarditis.[16] Our failure to find hemopericardium due to tuberculosis or uremia may be due to the fact that the effusions in these conditions were not of sufficient magnitude to be a direct or contributing cause of death, a requisite for inclusion in this study. Furthermore, frank blood in the pericardial sac is rare in uremia and tuberculosis although blood-tinged effusions are common.[6]

Since the pericardium behaves as an inelastic sac when acutely distended with blood, symptoms are closely related to the volume of the fluid. Kuno[17] demonstrated in 1917 that when the amount of fluid in the pericardial sac exceeds a critical level, the arterial blood pressure falls abruptly. He also demonstrated that elevation of the venous pressure restores the circulation, indicating that circulatory failure is due to interference with the venous inflow to the heart. Deductions from animal experiments suggest that the normal human pericardial sac can tolerate from 80 to 100 ml. of fluid without symptoms of cardiac tamponade.[18] Accumulations of 200 ml. or more are likely to produce symptoms,[19] and over 300 ml. are likely to prove fatal.[20] In our study, sixty of the eighty-nine (67.4 per cent) had over 200 ml. of blood in the pericardial sac while twenty-nine (32 per cent) had 200 ml. or less.

Gradual accumulations of blood in the pericardial sac permit a longer survival time and increase the likelihood of clinical recognition of the effusion. Massive hemopericardium is not necessarily fatal; spontaneous recovery from this complication has been observed in myocardial infarction,[21,22] dissecting aneurysm[23] and traumatic (bullet) perforation of the heart.[24] Gradual accumulations of fluid are frequent in those cases due to blood dyscrasia with coagulation defects.

Diagnosis: Pericardial effusion should be suspected when the following develop in a critically ill patient with a known provocative disease: evidences of increased venous pressure, lowering of the arterial and pulse pressure, a paradoxical pulse, an increase in the area of cardiac dullness and muffled heart tones. A friction rub may be present and may persist even when the effusion is massive.[25] The studies of Williamson[26] have shown that, contrary to general opinion, effusions produce comparatively little displacement of the heart, the fluid tending to accumulate in the inferior and lateral recesses of the sac. The electrocardiogram may be a helpful adjunct in diagnosis. The pattern that is suggestive of pericarditis includes low voltage, T wave inversion or S-T segment elevation. Various combinations of these changes may occur in several or all leads. Such changes when considered along with the clinical findings may be diagnostic. Although routine roentgenograms are seldom diagnostic, specialized technics such as the carbon dioxide angiocardiogram may give information of confirmatory value.[27]

Treatment: Aspiration of an acute pericardial effusion may be life saving. The procedure should be performed with caution, preferably in the apical or subxphoid region. The use of a continuous recording electrocardiogram

during the procedure is an aid in recognition of contact of the needle with the heart. Experiments by Cooper et al.[28] in dogs suggest that intravenous saline infusions are of value in maintaining the blood pressure despite a compressing pericardial effusion. The effect is immediate and persists for several minutes. Epinephrine, ephedrine sulfate or norepinephrine combined with intravenous saline solutions aided in maintaining systemic blood pressure in experimental studies performed by Cooley and Brockman.[29] Such temporary expedients may prolong the patient's life, providing the time needed to prepare for and to perform more definitive therapy.

Summary

One hundred five cases of nontraumatic hemopericardium were encountered among 21,000 consecutive autopsies at the Los Angeles County Hospital. The causes in order of frequency were acute myocardial infarction, sixty-three and ruptured aneurysm, thirty-five, of which thirty were of the dissecting type. There were four syphilitic aneurysms and one mycotic aneurysm of a coronary artery. Hemopericardium was the result of metastatic carcinoma in four and a blood dyscrasia in three cases.

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Pericarditis in Children*

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A REVIEW of the English literature of the last decade failed to reveal a comprehensive article on pericarditis in children except for the discussion of this topic in two recent texts on pediatric cardiology.[1,2] Several publications on individual disease entities affecting the heart do refer to pericarditis as part of the picture, but none of these discusses all causes of pericardial involvement in one publication.[3–7]

A number of excellent review articles on pericarditis in adults are available but these give only scanty attention to children.[8–10] It seemed, thus, worthwhile to discuss our own experiences with pericarditis in children in order to emphasize the particular etiologic factors involved and to point out the pertinent clinical features.

MATERIAL

The records of the patients with the diagnosis of pericarditis admitted to the Children's Hospital within the period of 1949 to 1959 were reviewed. A number of patients with rheumatic fever admitted directly to the House of the Good Samaritan Division of the Children's Medical Center have not been included in this study in order not to overemphasize the relative frequency of rheumatic fever in the cause of pericarditis. This arbitrary decision may, indeed, have resulted in underemphasizing rather than overstating the importance of rheumatic fever. Disease states in which terminal pericardial involvement was clearly secondary to other well recognized entities (i.e., metastatic tumors, uremia) were also excluded from the study. Finally, postoperative pericardial involvement, which belongs more in the realm of surgical complications, will also be omitted from this discussion.

The diagnosis of pericarditis was based upon the presence of at least one of the following criteria: (1) autopsy evidence of pericarditis; (2) pericardial fluid obtained by paracentesis or thoracotomy and (3) definite friction rub heard by several observers. A number of patients suspected of having pericarditis had to be eliminated from the study since they did not fulfill the relatively stringent criteria cited, in that a friction rub was only transiently heard by one observer, or the diagnosis of pericarditis was based on radiologic or electrocardiographic evidence alone.

The thirty-two patients included in the study are classified according to etiology in Table I.

RESULTS

1. PURULENT PERICARDITIS

As indicated in Table I pyogenic infection, together with rheumatic fever, has been the most frequent cause of pericarditis in children.

The pertinent features of this group are summarized in Table II. It may be seen that our patients varied in age from six weeks to seven years. In one patient (Case 2) with generalized sepsis, who died within twenty-four hours after admission, the presence of pericardial involvement was not recognized except at autopsy. In two others (Cases 3 and 6) the discovery of the friction rub led to the diagnosis. In two additional children (Cases 1 and 4), pulsus paradoxus was noted in addition to marked cardiac enlargement. In the final child (Case 5) the presence of severe chest pain, relieved by sitting up, together with the marked cardiomegaly, led to the proper diagnosis.

Physical Findings: Evidences of right-sided failure were noted in all in whom the diagnosis was made. The heart sounds were specifically observed to be normal in intensity in two patients (Cases 3 and 6) both of whom had fibrinopurulent pericarditis without large accumulation of fluid. Two additional patients had gallop rhythm. A systolic murmur was heard in the patient with transposition of the great arteries and transiently in one of the others (Case 6). Interestingly enough, in four of five patients for whom blood pressure measurements were available, the systolic pressure was found to be normal, although in three of these, pulsus paradoxus was noted. Tachycardia, ranging from 150 to 165 per minute, was present in all.

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TABLE I
Etiologic Classification of Pericarditis in Children

Type	No. of Patients
Purulent	6
Rheumatic	6
Rheumatoid	5
Acute benign	4
Miscellaneous	11
Congenital hypoplastic anemia	2
Cooley's anemia	1
Tuberculosis	2
Disseminated lupus	1
Glycogen storage disease	1
Friedreich's ataxia	1
Ulcerative colitis	1
Endarteritis	1
Chronic nonspecific	1
Total	32

Roentgenograms and electrocardiograms were available in every patient but the one baby with a twenty-four hour admission (Case 2). All roentgenograms showed cardiac enlargement and on fluoroscopy feeble pulsations were noted. The electrocardiograms all showed S-T and T wave changes.

Associated Diseases: Among the associated diseases were pneumonia (Cases 1 and 4), pyelonephritis, osteomyelitis and tonsillitis. Temperatures ranged from 99.6 to 106°F. Leukocytosis was noted in all, with counts between 20,000 and 35,000 per cu. mm. in four patients. Staphylococcus aureus was cultured from the pericardium of one patient postmortem. In a second child the same organism was obtained from the osteomyelitis wound (Case 6). In a third patient an x-ray picture was characteristic of staphylococcal pneumonia. Finally, a fourth child had Escherichia coli organisms in the urine (Case 2). It is worth noting that all patients had antibiotics prior to pericardial tap.

Therapy: Four of the six patients received combined chloramphenicol and erythromycin therapy in dosages ranging from 40 to 100 mg. per kg. The recommended dosage today is 100 mg. per kg. of chloramphenicol and 40 to 50 mg. per kg. of erythromycin. These two antibiotics in combination delay the appearance of resistant forms of staphylococci.

One patient received penicillin and streptomycin parenterally and Gantrisin® by mouth. In addition, the pericardial sac was irrigated with penicillin and streptomycin. When penicillin treatment is indicated, a minimum of three to four million units daily should be used and the addition of probenecid will help obtain a higher blood level of penicillin.

The patient (Case 2) whose pericarditis was not clinically recognized received Furadantin,® penicillin and streptomycin for his urinary tract infection.

Three patients in this series failed to survive. One (Case 2) died before his illness could be diagnosed. The second (Case 3) had severe associated congenital heart disease (transposition of the great arteries) and the third (Case 1) had transient cardiac arrest during pericardiotomy and died one day postoperatively. The other three patients made a good recovery and were completely normal on follow-up examinations.

2. RHEUMATIC PERICARDITIS

There were six patients in this series whose pericarditis was due to rheumatic fever. Table III indicates some of the important features of their illnesses. In four of the six children this was the initial attack of rheumatic fever. The onset of the rheumatic episode was within two weeks prior to admission in two patients; the other four had had symptoms for six weeks to five months prior to admission to the hospital. A pericardial friction rub first suggested the diagnosis of pericarditis in every patient. In addition, chest pain, alleviated by leaning forward in the sitting position, was also present in two patients.

Physical Findings: All of these children presented with evidences of pulmonary congestion, presumably indicating left-sided failure, in addition to obvious right-sided failure with increased venous pressure and an enlarged liver. Every child in this group had an elevated antistreptolysin titer. The murmur of mitral regurgitation plus a short mid-diastolic rumble were present in all patients at the time of admission. Two of the six patients also had a murmur of aortic regurgitation. Pulsus paradoxus was not present in any member of this group; consequently, it was assumed that pericardial tamponade was not present. Since the diagnosis of rheumatic fever was clear, no paracentesis was performed in any of these children.

All six of these patients showed moderate to marked cardiac enlargement by roentgenogram. Three were also reported to have passive congestion of the lung fields. The electrocardiogram showed S-T and T wave changes

TABLE II
Purulent Pericarditis

Case and Age	Manifestations of Pericarditis	Electrocardiogram S-T and T Wave Changes	Associated Disease	Previous Antibiotic Therapy	Pericardial Findings	Therapy	Culture	Outcome
(1) 1 yr.	Pulsus paradoxus and cardiomegaly	+	Pneumonia, ? staphyloccoccal	Penicillin	Cloudy, serous fluid	Chloromycetin and erythromycin	Negative	Died
(2) 6 wk.	Not suspected clinically; diagnosed at autopsy	Not performed	Pyelonephritis, following cystostomy for congenital genitourinary anomaly	Furadantin, penicillin and streptomycin	Thick and adherent pericardium; myocardial necrosis (autopsy)	None	E. coli in urine	Died
(3) 1 yr.	Friction rub and cardiomegaly	+	Transposition of great arteries	Terramycin, achromycin, penicillin and streptomycin	Fibrinopurulent pericarditis (autopsy)	Chloromycetin and erythromycin	Staph. aureus (postmortem)	Died
(4) 5 mo.	Pulsus paradoxus and cardiomegaly	+	Bronchopneumonia	Penicillin	120 cc. of thick, purulent material	Chloromycetin and erythromycin	Negative	Recovered
(5) 7 yr.	Chest pain and cardiomegaly	+	Tonsillitis	Penicillin and streptomycin	250 cc. of thick, purulent material	Penicillin and streptomycin irrigations Penicillin, streptomycin and gantrisin	Negative	Recovered
(6) 4 yr.	Pulsus paradoxus, cardiomegaly and friction rub	+	Osteomyelitis	Penicillin, streptomycin, chloromycetin, and erythromycin	Shaggy pericardium; fibrinous exudate; 120 cc. of fluid removed	Penicillin, chloromycetin and erythromycin	Staph. aureus from osteomyelitis	Recovered

TABLE III
Rheumatic Fever

Case and Age	History of Previous Attack	Duration of Symptoms before Admission	Manifestations of Pericarditis	Congestive Heart Failure	Antistreptolysin Titer	Murmur	Therapy	Outcome
(7) 11 yr.	+	2½ mo.	Friction rub and cardiomegaly	+	500	Mitral systolic, mitral and aortic diastolic	Aspirin	Died
(8) 10 yr.	−	6 days	Friction rub, chest pain and cardiomegaly	+	>1,000	Mitral systolic and diastolic	Steroids	Recovered
(9) 12 yr.	+	5 mo.	Friction rub, chest pain and cardiomegaly	+	>1,000	Mitral systolic and diastolic	Aspirin and steroids	Recovered
(10) 6 yr.	−	10 days	Friction rub and cardiomegaly	+	833	Mitral systolic and diastolic	Steroids	Recovered
(11) 10 yr.	−	6 wk.	Friction rub and cardiomegaly	+	>1,000	Mitral systolic, mitral and aortic diastolic	Steroids	Died
(12) 11 yr.	−	4 to 5 mo.	Friction rub and cardiomegaly	+	>1,000	Mitral systolic and diastolic	Aspirin	Recovered

indicative of myocarditis and/or pericarditis. The friction rub was present from one to two and a half weeks in the four patients who survived. One of these (Case 8) had an exacerbation of rheumatic fever, with recurrence of the pericarditis, when steroid therapy was discontinued after a four month course.

Fatal Cases: Two of the six died in severe congestive failure (Cases 7 and 11). At autopsy an adherent pericardium with fibrinous and vascular proliferation, and changes in the mitral and aortic valves with marked myocardial disease were seen in both. One of them also had severe "rheumatic pneumonia." It is interesting to note that of the two patients who died, one received no steroid treatment at all and the other received it for less than twenty-four hours before death.

Therapy: As indicated in Table III, two of the patients were treated with aspirin alone. One child was treated with a combination of aspirin and steroids. Three patients received steroids alone. One of them (Case 11), however, received the drug for only twenty-four hours prior to death. In addition, of course, they all received penicillin and anticongestive measures.

The treatment of rheumatic fever today is still a subject of controversy. In our opinion these severely ill children with rheumatic pancarditis can be treated more effectively with steroids than with salicylates, if the steroid dosage is adequate, that is, 60 mg. of prednisone daily or its equivalent. The duration of hormone therapy must be individualized, according to the clinical response of the patient.

In addition, anticongestive measures and penicillin, first in therapeutic and later in prophylactic doses, should unquestionably be administered.

3. RHEUMATOID PERICARDITIS

Five children in this group had rheumatoid pericarditis (Table IV). The diagnosis was based upon the nature of joint involvement, presence of a typical skin rash, temperature chart and natural history of the disease. Specific features diagnostic of other collagen diseases were absent. Pericarditis was recognized on the basis of a friction rub.

Clinical Features: The ages varied from fourteen months to eleven years. All patients but one were in the initial episode of rheumatoid arthritis. No pulsus paradoxus was present; thus, no pericardial tap was performed. One patient (Case 13) had rales bilaterally and the x-ray picture suggested passive congestion of the lung fields. Another patient (Case 14) showed tachypnea with hepatomegaly. The chest film showed passive congestion and bilateral pleural effusion. Thus, although pure right-sided failure suggesting cardiac tamponade was not seen these two children may have had left-sided failure.

TABLE IV
Rheumatoid Pericarditis

Case and Age	History of Previous Attack	Manifestations of Pericarditis	Electrocardiogram S-T and T Wave Changes	Congestive Heart Failure	Antistreptolysin Titer	Murmur	Therapy	Outcome
(13) 11 yr.	−	Chest pain, friction rub and cardiomegaly	+	+	<50	None	Steroids	Recovered
(14) 4 yr.	−	Chest pain, friction rub and cardiomegaly	+	−	<50	None	Aspirin	Died
(15) 5 yr.	+	Chest pain, friction rub and cardiomegaly	+	+	Not performed	None	Aspirin and steroids	Recovered
(16) 3 yr.	−	Chest pain, friction rub and cardiomegaly	+	−	<50	Grade 1 systolic, apical	Aspirin, butazolidine and steroids	Recovered
(17) 14 mo.	−	Chest pain, friction rub and cardiomegaly	+	−	<50	Grade 2 systolic, lower left sternal border	Steroids	Recovered

TABLE V
Idiopathic Benign Pericarditis

Case and Age	Manifestations of Pericarditis	Electrocardiogram S-T and T Wave Changes	Congestive Heart Failure	Lung Fields on Roentgenogram	Outcome
(18) 2 yr.	Friction rub and cardiomegaly	+	−	Pleural effusion and pneumonitis	Recovered
(19) 6 yr.	Chest pain, friction rub and cardiomegaly	+	−	Pleural effusion	Recovered
(20) 14 yr.	Chest pain and friction rub	+	−	Clear	Recovered
(21) 6 yr.	Chest pain, friction rub and cardiomegaly	+	−	Pneumonitis	Recovered

In contrast to the patients with rheumatic fever, none of these children showed significant murmurs. Cardiomegaly was evident by roentgenogram. S-T and T wave changes were seen in the electrocardiogram.

The duration of the pericardial friction rub was less than one week in all patients. By three weeks the heart size had returned to normal in all but one of the survivors. This child (Case 15) had persistent mild cardiomegaly.

Therapy: Four of five patients were treated with steroids; two of these received aspirin simultaneously. One child was treated with aspirin alone. Antibiotics were given to all but one patient (Case 15).

Only one child (Case 14), the patient not treated with steroids, died during the episode associated with pericarditis. This patient had hemorrhagic manifestations, including a profuse nosebleed and hematemesis, twenty-four hours before death. Autopsy revealed over 300 cc. of blood in the pericardial sac.

The initial dosage of steroids is suggested as 60 mg. of prednisone daily. Salicylate therapy should achieve a blood level of 30 to 40 mg. per

cent; usually an aspirin dosage of 40 mg. per pound is required.

4. IDIOPATHIC BENIGN PERICARDITIS

Four patients had to be classified as having idiopathic benign pericarditis principally because of the absence of any other recognizable etiologic agent and because the clinical profile and course fitted this diagnosis (Table v). No viral studies were performed on these patients since they were all admitted to the hospital prior to the time when technics were commonly available for identifying the specific viruses involved.

Clinical Features: All patients had a friction rub, two had associated pleural effusion and two showed radiologic evidences of pneumonitis. All had a cough and fever for some time prior to recognition of pericarditis. There was, however, no evidence of a previous attack of pericarditis in these children, nor are we aware of recurrence later, although we have not specifically followed these patients after their initial illness. Chest pain was severe in three, and one two year old boy (Case 18) complained of abdominal pain. The sedimentation rate was elevated in two patients. In one child (Case 20) there was a significant murmur. This boy was a patient at our cardiac clinic for several years, and the diagnosis clinically and at catheterization was idiopathic pulmonary regurgitation.

Pericardial tamponade was not suspected in any of these patients since congestive failure was uniformly absent and pulsus paradoxus was not noted in any instance. No pericardial tap was performed.

5. MISCELLANEOUS

Blood Dyscrasia: Three children had blood dyscrasias (Table vi). The first (Case 22) had Cooley's anemia and hemosiderosis due to multiple transfusions. Splenectomy had been performed two years before the onset of pericarditis.[11] In the course of three months the child had two separate episodes of pericarditis, neither of which caused tamponade. The pericardium was described at biopsy as being diffusely adherent, edematous and thickened. No iron pigment was noted on microscopic examination.

The second patient (Case 23) was a girl who survived to the age of sixteen with congenital hypoplastic anemia. Clinical hemosiderosis had developed in this patient, too. Splenectomy had not been performed. Pericarditis had not been diagnosed clinically, but at autopsy she was found to have 125 cc. of straw-colored fluid in the pericardial sac. Microscopic examination showed iron pigment in the epicardium and myocardium.

The third child (Case 24) had congenital hypoplastic anemia and hemosiderosis. Splenectomy had been performed four years before her death.[11] She contracted chicken pox with encephalitis, and during this episode showed progressive enlargement of the cardiac silhouette, with signs of right-sided failure and pulsus paradoxus of 25 mm. Hg. Pericardiostomy was performed and over 100 cc. of straw-colored fluid was removed from the pericardial sac. The patient improved temporarily, only to die of pulmonary edema twelve days after pericardiostomy. Permission for autopsy was not obtained.

Tuberculous Pericarditis: There were two patients in whom the diagnosis of tuberculous pericarditis was made (Table vi). One of these, a fourteen year old boy with positive acid-fast smear and guinea pig inoculation (Case 26), was of particular interest from several points of view. First, he was the only one of the entire group who showed evidences of constrictive pericarditis. Second, the constrictive phenomena developed under our observation through a period of six months, during which repeated taps were performed to evacuate rapidly accumulating pericardial fluid. The diagnosis of tuberculous pericarditis in the second youngster (Case 25) was based on the circumstantial evidences of close exposure to tuberculosis, development of pulmonary involvement and good response to specific therapy. At the time of the first pericardial tap, which failed to show acid-fast organisms, he already had received a small amount of streptomycin and para-aminosalicylic acid. As may be seen from Table vi both these youngsters had evidences of tamponade with definite pulsus paradoxus. The fluid was cloudy in both instances.

Disseminated Lupus Erythematosus: In regard to the patient with disseminated lupus erythematosus (Case 27) it may be worth mentioning the pericardial fluid accumulation was the only major manifestation of the disease at the time of hospitalization. Pains in the joint, without objective evidence of arthritis, preceded the appearance of pericarditis by four months. It should also be pointed out that the pericarditis was originally thought to be of rheumatic origin,

TABLE VI
Miscellaneous Causes

Case and Age	Diagnosis	Manifestations of Pericarditis	Pericardiotomy	Comments
(22) 14 yr.	Cooley's anemia	Chest pain, friction rub and cardiomegaly	Edematous adherent pericardium without iron deposits	Splenectomy 2 yr. before onset of pericarditis; repeated episodes of pericarditis
(23) 16 yr.	Congenital hypoplastic anemia	Not diagnosed clinically	Not performed	No previous splenectomy; autopsy revealed 125 cc. straw-colored fluid in pericardium; iron deposits in myocardium and pericardium
(24) 8 yr.	Congenital hypoplastic anemia	Cardiomegaly, pulsus paradoxus and tamponade	Clear, straw-colored fluid (100 cc.)	Splenectomy 4 yr. prior to pericarditis; chicken pox encephalitis and pericarditis at same time; died; no autopsy
(25) 19 yr.	Tuberculosis	Chest pain, friction rub, cardiomegaly, pulsus paradoxus and tamponade	Thin, smoky fluid (500 cc.)	Tuberculous exposure; tuberculin test changing to positive; pneumonitis
(26) 14 yr.	Tuberculosis and constrictive pericarditis	Pulsus paradoxus, cardiomegaly and tamponade	Repeated removal of cloudy, yellow fluid (200–300 cc.)	Positive acid - fast smear, guinea pig inoculation; pericardiectomy performed for constrictive pericarditis 6 months after onset.
(27) 11 yr.	Disseminated lupus erythematosus	Friction rub, cardiomegaly and tamponade	Small amounts of serosanguineous fluid, needle aspiration	Pain in the joints and positive lupus erythematosus cell preparation; pericarditis subsided spontaneously
(28) 2 mo.	Proliferative endarteritis and myocardial infarction	Not diagnosed clinically	Not performed	Autopsy showed panarteritis; small healing myocardial infarction; subacute fibrinous pericarditis
(29) 2 yr.	Glycogen storage disease	Cardiomegaly and pulsus paradoxus	Not performed	Autopsy showed thickened, adherent pericardium with 170 cc. of sterile fluid
(30) 14 yr.	Friedreich's ataxia	Chest pain, cardiomegaly, pulsus paradoxus and tamponade	Straw - colored fluid (250 cc.)	Autopsy showed myocarditis and fibrinous obliterative pericarditis
(31) 13 yr.	Ulcerative colitis	Friction rub and chest pain	Not performed	Patient had erythema nodosum, pleurisy and pericarditis with ulcerative colitis
(32) 10 yr.	Congenital heart disease (pulmonic stenosis)	Cardiomegaly and pulsus paradoxus	Aspiration of 400 and 150 cc. of fluid on 2 occasions	At surgery, pericardium was diffusely adherent; nonspecific, chronic inflammation on microscopic examination

despite the absence of murmurs. For this reason, steroid treatment was instituted in another hospital without any alleviation of symptoms and even progressive tamponade. Rapid tapering of cortisone dosage was accompanied by gradual clearing of the pericardial effusion.

Friedreich's Ataxia: The patient with Friedreich's ataxia (Case 30) is the only one in the

literature, to our knowledge, with pericarditis as well as myocarditis. This boy was first reported on by one of us in a publication ten years ago.[12] It is interesting to note that he survived the initial episode and died ten years later with congestive failure and pericardial fluid accumulation.

Pulmonic Stenosis: The last patient had severe pulmonic stenosis with an intact ventricular septum. A pericardial tap was performed because of marked pulsus paradoxus and resulted in evacuation of 400 cc. and 150 cc. of clear fluid on two separate occasions. At the time of pulmonary valvotomy the pericardium was found to be thick and adherent. The microscopic picture was one of chronic inflammation. No fluid accumulation occurred since successful valvotomy.

Comments

The most frequent etiologic entities associated with pericarditis in this group of children were rheumatic fever, rheumatoid arthritis, bacterial infection and idiopathic benign pericarditis. The latter entity was relatively less common whereas rheumatic fever, rheumatoid arthritis and suppuration were seen more frequently than in adults.[8]

Differential Diagnosis: The problem of differentiating pericarditis from myocardial infarction, a difficult challenge in internal medicine, does not occur frequently in children. It is replaced by the necessity of differentiating between pericarditis with effusion and myocarditis with cardiac dilatation. In those children who do not have a pericardial friction rub the distinction may not be possible on clinical grounds alone. The rapid development of cardiac enlargement may point equally well to myocarditis as to pericarditis. Muffled heart sounds may be present or absent in either condition. The globular shape of the heart on roentgenogram, with widening of the base as the patient is tilted to a horizontal or head down position, is common to both conditions. The finding of diminished pulsation on fluoroscopy also may be seen in myocardial disease as well as with pericardial effusion. The electrocardiographic changes of pericarditis are probably due to subepicardial myocarditis, the pericardium itself being electrically inactive.[13] It is, therefore, not surprising that the electrocardiogram is also of no value in the differentiation of the two conditions. The serial changes in S-T segments and T waves are much the same in the two diseases. The Q-T interval, corrected for rate by Bazett's formula, is said to be prolonged in myocarditis and shortened in pericarditis. However, a number of the patients discussed previously showed a Q-Tc which was short initially, without digitalis administration, then became prolonged at a later stage. This sequence of changes has been previously described for both myocarditis and pericarditis.[14]

A chest roentgenogram revealing a very large cardiac silhouette without evidence of passive engorgement of the lung fields appears to be the most useful radiologic criterion in differentiating between pericardial effusion and myocarditis. It is believed that a heart which is maximally enlarged due to myocardial involvement probably will have associated pulmonary congestion. The presence of pulsus paradoxus of less than 10 mm. Hg is probably physiologic. Values between 10 and 20 mm. Hg have been recorded, particularly postoperatively, in patients who did not have appreciable pericardial disease. Pulsus paradoxus of greater than 20 mm. Hg is highly suggestive of pericardial effusion with tamponade.

By passing a cardiac catheter into the right atrium and fluoroscopically visualizing the tip against the right heart border, it is possible to determine the presence or absence of pericardial fluid.[15] Intravascular injection of contrast media, either radiopaque dye or carbon dioxide, will also distinguish the shadow of fluid in the pericardial sac.

Recent experience with the fluoroscopic image intensifier has suggested that the improvement in definition over conventional fluoroscopy permits adequate delineation of the heart border within the fluid-filled pericardium. This procedure alone, without additional cardiac catheterization, may prove to be a most useful tool in demonstrating the presence of pericardial effusion, if the results prove to be consistent as experience accumulates.

Pericardiocentesis: When it becomes necessary to remove fluid from the pericardium, either for diagnostic studies or relief of tamponade, a small thoracotomy incision is preferred in this hospital to the blind approach. This preference is based, principally, on the high incidence of primary myocardial disease in children, as compared with pericardial fluid accumulation and, thus, the potentially greater risk of paracentesis in children as compared with adults.

In any child suspected of having purulent pericarditis pericardial fluid should be withdrawn for culture. Since tamponade is frequently seen in those who have bacterial pericarditis, surgical exploration of the pericardial sac offers the additional advantage of more adequate drainage.

Cardiac tamponade was not seen in this series of patients with idiopathic pericarditis or rheumatic fever. One patient with rheumatoid arthritis died because of a large hemorrhage into the pericardial sac. There are reported cases of tamponade in all three of these disease entities but they are uncommon.

In the recognition of tamponade it is important to recall that the heart sounds may not be muffled, the apex beat may not be damped, ventricular impulse on fluoroscopy may not be abolished and orthopnea is not always present.[16] Pulsus paradoxus may be found in patients in congestive failure, with peripheral vascular collapse, and in patients with obstructive disease of the lower respiratory tract. However, in those patients with respiratory disease in whom highly negative intrathoracic pressures develop the distention of the neck veins becomes prominent on expiration rather than on inspiration.[17] Constant distention of the neck veins is said to be more common in congestive failure while pulsating neck veins, with the patient in the upright position, are more characteristic of tamponade. Ankle edema and ascites are said to be uncommon in cardiac tamponade.[16]

Treatment: The medical treatment of patients with pericarditis without tamponade depends a great deal upon the cause of the disease. In our opinion, not shared by all workers in the field, patients with rheumatic pericarditis should be treated with steroids. We can find no conclusive evidence indicating any advantage of hormonal treatment in patients with idiopathic benign pericarditis. In patients with pericarditis associated with rheumatoid arthritis, because of the chronicity of the disease and lack of a high mortality, we are considerably more reluctant to use steroids than in patients with rheumatic fever.

No specific treatment is available in the other etiologic entities except acute suppurative and tuberculous pericarditis. Patients should be treated with the appropriate specific drugs. Surgical relief of the effusion should be contemplated if tamponade occurs and one has to bear in mind the possibility of constrictive pericarditis following the acute phase.

Summary

The experience with pericarditis at the Children's Hospital Medical Center of Boston during the past ten years is reviewed. The clinical features of the most common etiologic groups, rheumatic fever, rheumatoid arthritis, bacterial infection and the benign idiopathic group, are presented. The problem of differentiating between pericardial effusion and cardiac dilatation is considered, and the most helpful methods of diagnosis are discussed. The therapy of the more frequent etiologic forms is indicated.

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Pericarditis in Tropical Diseases*

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IN ANY DISCUSSION of pericarditis in tropical medicine one must first establish the scope of disease included. The practice of internal medicine in the tropics includes both cosmopolitan disease and that peculiar to warm climates, and there is little need for differentiation of the two groups. Outside the tropics "tropical medicine" has a variable connotation. It usually includes parasitic and other infectious diseases closely related to those of warm climates, even if found only or predominantly in colder climates. For this reason textbooks of tropical medicine include such diseases as fish tapeworm, which is common in Scandinavia, as well as bacterial, viral and fungal disease closely related biologically to diseases occurring in the tropics but themselves occurring elsewhere in the world. Such diseases as tularemia, coccidioidomycosis and brucellosis are frequently included. At the same time cosmopolitan diseases more prevalent in the tropics than elsewhere, such as tuberculosis and syphilis, are not included. The present disdiscussion will, of necessity, recognize the broad and loose definition of tropical medicine.

In general, acute and chronic forms of pericarditis as distinctive primary clinical pericarditic pictures are unusual in tropical diseases. Indeed, the indices of texts on tropical medicine do not usually include a listing of pericarditis as such. Pericarditis in this kind of disease is, therefore, rare and in most listings of types of pericarditis these are included in the general discussions as "unusual" or "other" types.

CLINICAL PICTURE AND DIAGNOSIS

The diagnosis of acute pericarditis is, in general, not as clear-cut and simple as the precise diagnostic criteria we utilize would indicate.[1] Herrmann[2] noted a twofold difference between the incidence at necropsy and clinical incidence of acute pericarditis. Even if one allows for terminal episodes it is obvious that pericarditis is often undiagnosed. The diagnostic criteria are either not met or not recognized. In a study of 240 patients previously reported[3] the author noted that among the multiplicity of factors involved with adequate diagnosis one was concerned with acute pericarditis as a part of a generalized clinical picture. Many patients having pericarditis associated with generalized infections are in this group. These patients display a general clinical picture with predominating symptoms and signs outside the area of the heart. The findings of acute pericarditis are likely to develop at a time considerably postdating the onset of illness and after the evolution of the primary clinical picture. The extra pericarditic symptoms may be striking and draw the attention of the patient and of the physician away from the heart. If the signs of pericarditis are not striking, they may be overlooked unless repeated examination is carried out. This is particularly true in tropical diseases in which pericarditis is not a frequent or important part of the clinical picture. Pericarditis as a clinical expression is uncommon, even in *African trypanosomiasis*, in which a severe myocarditis occurs as the result of invasion of the cells of the heart muscle and with which in experimental infections there is an associated exudative pericarditis. The same is true in *Chagas' disease* or South American Leishmaniasis; in which the heart is involved as a primary part of the clinical picture. Myocarditis, with heart failure, bundle branch block and other manifestations of involvement of the heart muscle is common; yet pericarditis as a clinical picture is rare.

In *Weil's disease* and *yellow fever* pericarditis may result from the uremia which is frequently part of these diseases. The pericarditis is of the type generally noted in acute uremia.

Generalized Infections Involving the Pericardium: In some infections generalized involvement

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of any or all organs may occur and involve the pericardium. This is true in the *typhus group*, *typhoid fever* and in *influenza*. In those in which metastatic spread may involve any or all organs from a primary site of infection, pericarditis, usually with little clinical expression, may appear. This is true in *bacillary dysentery*, in which myocarditis and pericarditis occur as so-called complications. In *brucellosis*, *melioidosis* and *actinomycosis* involvement of this type is noted. Even in *yaws* opalescent or porcelain patches are revealed in the pericardium at autopsy. In *echinococcus* infections the heart may be involved by hydatid cysts and the infestation may be seemingly localized to the heart. Rupture of cysts may produce acute pericarditis or pericardial effusion with the clinical findings of pericarditis.

Pericarditis by Extension from Lungs: Pericarditis may occur by contiguity from the lungs. A number of tropical infections cause involvement of the pericardium by such direct spread. *Pneumonic plague* thus involves the pleura and the pericardium with an inflammatory reaction in the area adjacent to the affected lung. In *tularemia* and in *actinomycosis* the same mechanism may be involved in addition to the previously mentioned generalized dissemination. Pericarditis may appear in *coccidioidomycosis* during the acute phase in the lungs. In geographic areas where this infection occurs, pericarditis of doubtful or unexplained origin warrants search for its cause. The skin test may be helpful along with the complement fixation and precipitin tests. The recovery of organisms from the sputum or pericardial fluid at times establishes the diagnosis.[4] In this type of pericarditis severe substernal pain with typical electrocardiographic changes and friction rub, as seen in acute benign pericarditis, has been described. In tularemia, in which pericarditis is apparently uncommon, effusion and the picture of constriction have been described as end results of acute tularemic pericarditis.[5]

Amebic Pericarditis: Involvement of the pericardium by contiguity of infection occurs occasionally in *amebic disease* of the liver. Rupture of abscesses of the liver most commonly occurs into the pleura, lung and peritoneum; rarely does such an abscess rupture into the pericardium. The infrequency of left-sided abscess is in part responsible for this rarity.[6] When rupture does occur, it is usually fatal, often in a very short period of time. Such symptoms as precordial pain, cyanosis, dyspnea and irregular pulse accompany tamponade and death. Clinical findings vary from this acute fulminating picture to a more chronic low grade one. In 1945, Kern[7] reported the case of a patient with amebic pericarditis secondary to liver abscess in which the picture of pericarditis dominated the clinical findings. Diagnosis was made by demonstration of "chocolate sauce" fluid.

In a review of the literature from 1885 to 1950, Carter and Korones[8] found only forty-four proved cases of suppurative pericarditis due to amebas. In addition, there were fourteen patients with suggestive but not proved evidence of amebic pericarditis. All instances were secondary to abscess adjacent to the pericardium in the liver or lung. The disease was successfully recognized during life in two of these patients; only one survived. Carter and Korones reported an additional instance in which diagnosis was made at surgery. Pericarditis with evidences of hepatic abscess should indicate the diagnosis. In fact, all indications of liver abscess are helpful when the unusual complication of amebic pericarditis occurs.

Summary

Pericarditis as a part of the clinical picture in so-called tropical diseases is rare. Pericarditis, when it does occur, usually develops as a part of a generalized clinical picture. The findings of pericarditis are often not striking or are overshadowed by other clinical findings. In some varieties, notably actinomycosis and amebiasis, the prognosis is poor.

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Case Reports

Cholesterol Pericarditis*

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In 1919, Alexander[1] reported a case of pericardial effusion with a "gold paint" appearance due to the presence of cholesterol crystals. Since this classic description, only a few additional cases have been reported. The present case is added to the literature because of its rarity and since it presents some other important features: (1) an unusually long duration of pericardial effusion, probably lasting eight years and possibly sixteen years; (2) striking freedom from symptoms for many years, in spite of a large pericardial effusion; and (3) apparent arrest after thoracotomy and pericardial biopsy.

CASE REPORT

On July 18, 1956, a forty-one year old aircraft manufacturing executive was admitted to the hospital with complaints of wheezing, shortness of breath and fatigue.

In 1940 he consulted a physician because of fatigue and was found to have a pericardial effusion. Three pericardial aspirations were performed. The patient recalled that the fluid was straw-colored. Bedrest was prescribed for ten months with a presumptive diagnosis of tuberculosis. Although he was told that the effusion was still present, he chose to return to work and has worked full time since then. He was admitted to the hospital in 1948 for treatment of a perirectal abcess, at which time an x-ray film of the chest was taken (Fig. 1, May 26, 1948). He was again hospitalized in 1949 for a perirectal abscess and had an incision of the abscess and saucerization of the fistula. From 1948 to 1955 he was seen regularly by his physician, who fluoroscoped him frequently and each time an enlarged cardiac shadow was demonstrated.

He felt well until about April 1956, when he began to note swelling of his legs, shortness of breath on exertion, fatigue, orthopnea and night sweats. He recalled a respiratory infection about December 1955, and again in April 1956. Varicose veins had been noted for one year. He worked until the day of his hospital admission although his symptoms had become progressively more severe.

Physical examination on admission revealed that the blood pressure was 100/78 mm. Hg in both arms and the pulse rate 72 per minute. No abnormality of the eyes, ears, nose or throat was noted. The thyroid gland was normal in size, but neck veins were distended. Cardiac dullness extended from the right mid-clavicular line to the left anterior axillary line. Cardiac sounds could barely be heard and precordial pulsation was not present. Peripheral pulses were normal and a paradoxic pulse was not present. The liver was palpable about 6 cm. below the right costal margin, did not pulsate, was moderately tender, firm and had a sharp edge. Signs of ascites were not present. Rectal examination was normal. Edema was present up to the knee level and severe varicosities, involving the superficial saphenous system, were present bilaterally.

Laboratory Data: Urinalysis, red cell count, hemoglobin, hematocrit, white cell count, differential, fasting blood sugar and urea nitrogen were normal. The Kline test was negative. Serum glutamic oxaloacetic transaminase was 26 units and the sedimentation rate (Wintrobe) 25 mm. per hour. L. E. cell study was negative on five occasions. C reactive protein was negative. Serum calcium was 9.4 mg. per cent, cholesterol 162 mg. per cent and cholesterol esters 88 mg. per cent. Thymol turbidity, serum bilirubin, alkaline phosphatase and cephalin flocculation were normal. Protein-bound iodine was 4.5 μg. per cent. A.S.O. titer measured 166 Todd units. Electrophoretic study showed a total protein of 7.95 gm. The various particles in per cent of total were: alpha globulin, 23 per cent; beta globulin, 21 per cent; alpha 2 globulin, 14 per cent; alpha 1 globulin, 10 per cent; albumen, 32 per cent; I^{131} uptake was 36 per cent in twenty-four hours and 20 per cent in six hours. I^{131} excretion was 58 per cent in twenty-four hours. The histoplasmin and coccidioidin skin tests were negative. The tuberculin skin test (P.P.D.) (0.001 mg.) was 1 plus.

The electrocardiogram dated July 19, 1956, is

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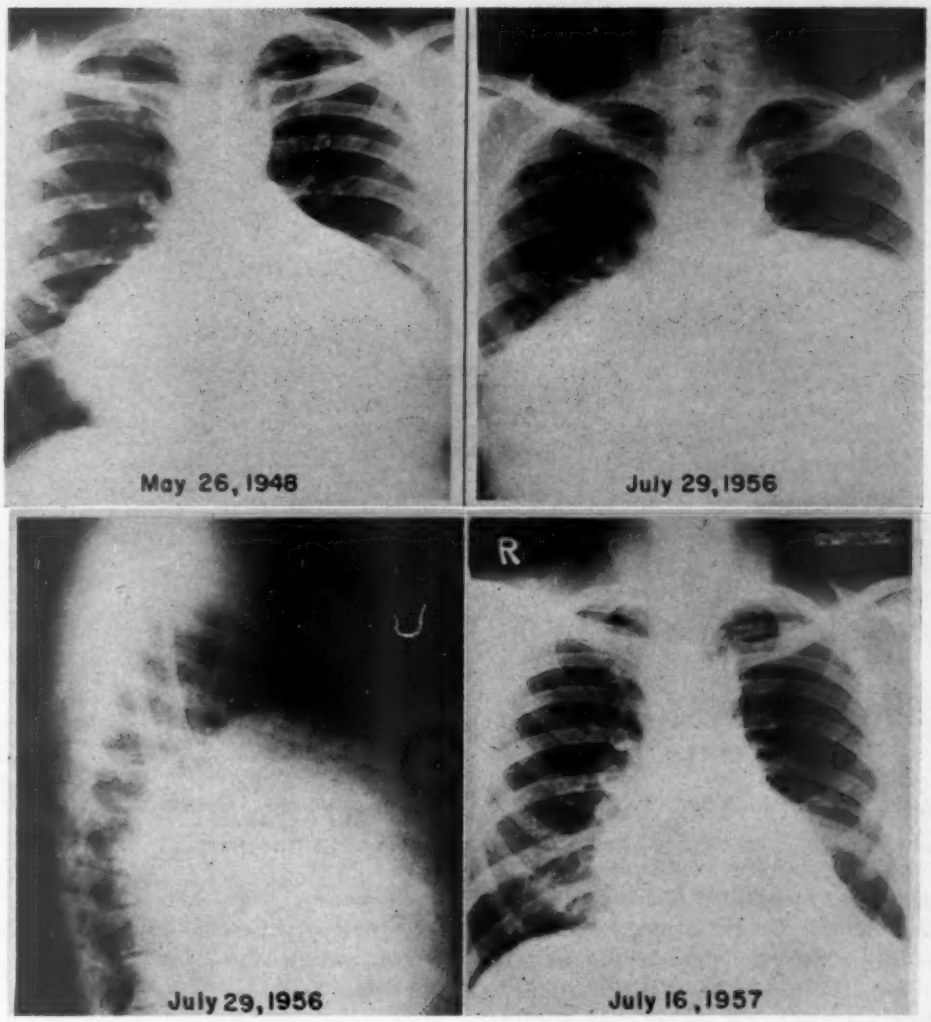


FIG. 1. Teleroentgenograms. Note the large cardiac silhouette present in 1948, the further increase in size apparent on the 1956 posteroanterior and lateral film, and the striking reduction seen in 1957 following surgery.

shown in Figure 2. Posteroanterior and lateral x-ray film of the chest, dated July 29, 1956, is shown in Figure 1. Venous pressure was 17.2 cm. of water in the right arm. Circulation time, arm-to-lung, was nine seconds by the ether method and the arm-to-tongue time was twenty seconds, using Decholin®.

On July 21, 1956, *pericardial paracentesis* was performed and 2,600 cc. of fluid removed. The fluid was the color of strong coffee, somewhat cloudy, and suspended in the fluid were innumerable tiny gold-colored flecks, giving it the appearance of gold paint. Examination of the pericardial fluid showed the specific gravity to be 1.022, and the cell count 11,623 with 43 per cent lymphocytes and 57 per cent segmented cells. Total protein was 6.9 gm. per cent. A smear for acid-fast bacillus was negative, as was a culture and guinea pig inoculation. Microscopic examination of of the centrifuged material showed numerous cholesterol crystals (Fig. 3).

Following aspiration, the patient felt well for about twenty-four hours, following which he began to have a temperature of 100 to 103°F., accompanied by chilly sensations. He was given procaine penicillin, 600,000 units twice a day, for five days.

He left the hospital on August 1, 1956, without being totally relieved, although he was somewhat improved. The fever gradually disappeared and there was nearly complete disappearance of edema of the lower extremities.

Further Course and Surgical Findings: On October 1, 1956, the patient had an episode of vomiting and diarrhea followed by daily temperature elevations to 100 to 102°F., which continued until he was rehospitalized on October 19, 1956. He experienced progressive dyspnea and orthopnea during the week prior to admission and ankle edema appeared three to four days prior to admission. Physical findings were essentially those of his previous admission.

On October 19 and October 21, 1956, pericardial aspirations were done with removal of 1,000 cc. of

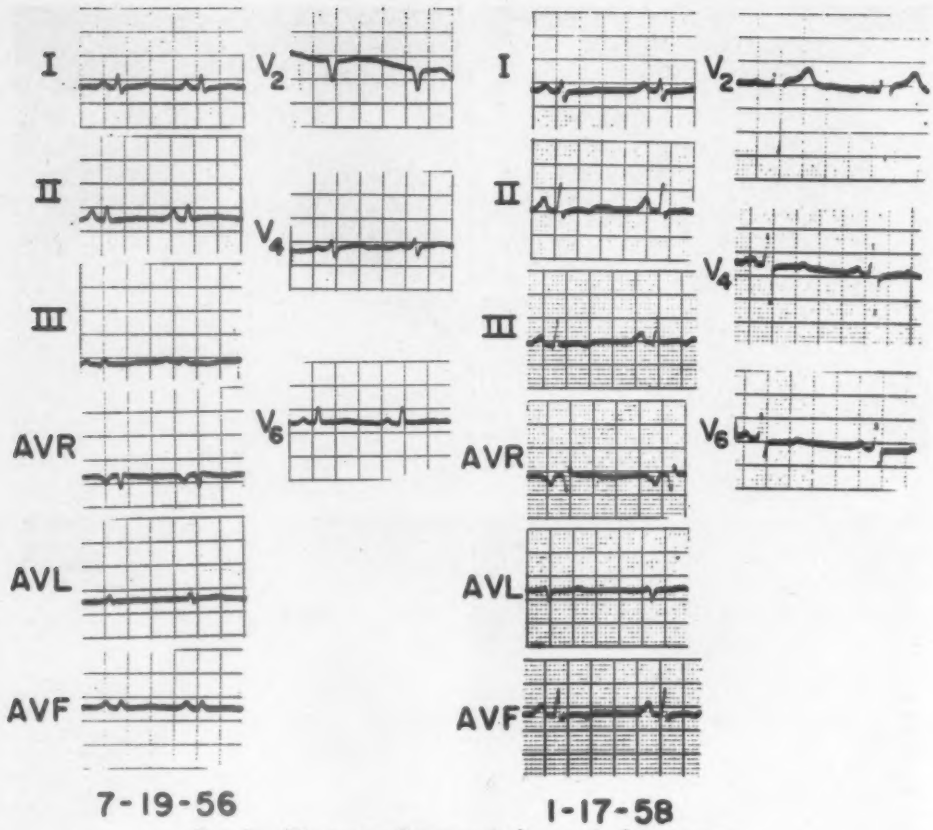


FIG. 2. Electrocardiograms before and after surgery.

fluid each time. On October 26, 1958, thoracotomy and pericardial biopsy were performed. *Laboratory tests on the pericardial fluid* removed at the time of surgery were as follows: Cholesterol crystals, numerous; sugar, 72 mg. per cent; total protein, 6.0 mg. per cent; chloride, 612 mg. per cent; specific gravity, 1.018; white blood cell count, 280 per cu. mm.; differential: polymorphonuclear leucocytes, 36 per cent; lymphocytes, 64 per cent; red blood cell count, 240,000 per cu. mm.; malignant cells, negative; total fat, 1,100 mg. per 100 cc.; culture, negative. On October 27, 1956, serum cholesterol was 160 mg. per cent and total fat, 1,200 mg. per 100 cc.

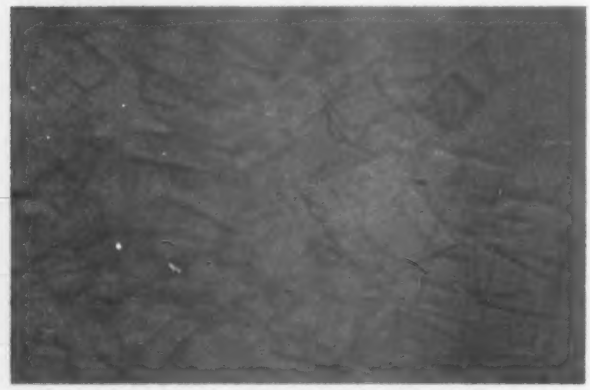
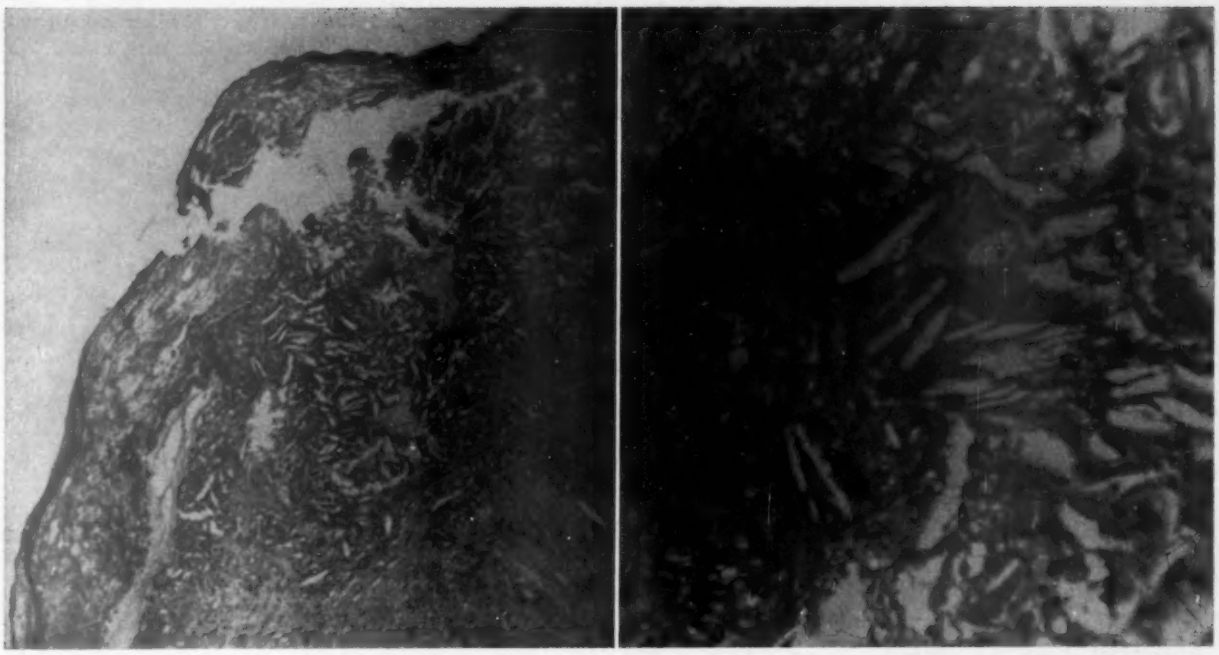


FIG. 3. Photomicrograph of centrifuged fluid from pericardial cavity showing cholesterol crystals.

Specimens for biopsy were taken from the epicardial and parietal pericardium and were stained for fungi by the Schiff technic. None was found. Microscopic examination of the tissue revealed proliferative fibrosis which, in some areas, revealed hyalinization. Foci of lymphocytes, plasma cells and foreign body giant cells were scattered through the tissue. There were tiny areas of hemorrhagic extravasation. Several thick-walled blood vessels of the capillary type were present. No tumor cells were seen. Cleft-like spaces characteristic of cholesterol deposition were present. No tubercles were seen and no acid-fast bacilli identified (Fig. 4).

Postoperatively the patient had daily fever but was dismissed from the hospital on November 10, 1956. During hospitalization, following surgery, he was given 400,000 units of procaine penicillin and 0.5 gm. of streptomycin twice daily for eleven days. He had a temperature of from 100 to 102°F. daily for six weeks following discharge. However, edema of the lower extremities, ascites and liver size diminished while he was still in the hospital and by March 1957 he was feeling well, worked full time and had only a trace of edema of the legs. By July 1957 the liver was no longer palpable and only an occasional trace of edema of the lower extremities was noted. No further symptoms have developed to date, and subsequent x-ray films of the chest show no change in cardiac size (film dated July 16, 1957, Fig. 1). The electro-



A B

FIG. 4. A, photomicrograph of visceral pericardium showing cholesterol clefts and fibrous thickening; hematoxylin and eosin ×100. B, high power photomicrograph showing cholesterol clefts and hyalinized fibrous tissue; hematoxylin and eosin ×44.

cardiogram continued to show abnormal T waves (Fig. 2, January 17, 1958).

COMMENTS

The etiology of cholesterol pericarditis is unknown. In three cases reported,[1,3,4] each author suggests myxedema as the etiology, but in none of the remaining cases has this been present. In our case there was no clinical evidence of hypothyroidism and the protein-bound iodine and I^{131} studies were normal. All authors have suspected tuberculosis, but in only one case[2] has the tubercle bacillus been found. In the case herein reported, a careful search for tubercle bacillus in the fluid, by smear, culture and guinea pig inoculation, was negative. In addition, biopsy tissue of pericardium, both visceral and parietal, showed nothing typical of tuberculosis. Review of the sections taken from the rectal fistula did not show characteristics of tuberculosis. Hemopericardium has been suggested as a possible cause and, indeed, some experimental support for this has been presented by Ehrenhaft,[10] who also demonstrated that the lipid fraction of blood more consistently produced a pericardial reaction when injected into the pericardium than did whole blood. This reaction, however, was not typical of cholesterol pericarditis. Idiopathic pericarditis of benign type is now frequently recognized, and occasionally has chronic manifestations.[11] Large asymptomatic pericardial effusions have been reported in two brothers,[13] and the fluid in one contained cholesterol crystals. The author suggested that the cholesterol crystals may have resulted from the very slow absorptive properties of the pericardium allowing slow degradation of lipoprotein complexes.

Five of the patients reviewed died,[2,4,7–9] but six were alive at the time they were reported. Of these, one[3] improved with administration of thyroid extract; the patient presented herein and one other[5] improved after thoracotomy and pericardial biopsy; another patient improved after repeated aspirations,[1] two[6,13] improved after pericardiectomy, and one[12] improved after aspiration and antituberculosis therapy. The removal of the entire parietal pericardium, if feasible, might remove the dangers of constrictive pericarditis. It is interesting to note, however, that none of the patients autopsied or surgically explored has shown constrictive pericarditis, so proof that this may result is still lacking.

A remarkable feature of this case is the duration of effusion. There is little doubt that the patient had continuous effusion from 1948 until surgery in 1956. It is possible that it was continuously present from 1940 to 1956 al-

though this cannot be documented. Some other reported cases[9,12,13] were also of long duration, but none beyond eight years. This case emphasizes the remarkable adaptability of the circulation to a slowly developing pericardial effusion.

The patient showed improvement following thoracotomy and biopsy. Why this occurred is not clear. The possibility that antibiotics, given postoperatively, could have influenced the course of the disease must be considered. This seems unlikely since he continued to have a daily fever for six weeks after all antibiotics were stopped.

None of the patients reported, as well as the present one, showed a significantly elevated serum cholesterol.

Summary

An unusual case of cholesterol pericarditis is presented and the literature reviewed. The etiology is still unknown and the treatment is not established.

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A Case of Traumatic Pericarditis with Chronic Tamponade and Constriction*

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THE ETIOLOGY of constrictive pericarditis often remains unknown even after a thorough clinical and pathologic study. Trauma is a well established although infrequent cause. McKusick[1] in 1955 cited eleven cases from the literature and contributed three more. Usually it is not even considered as a possibility. The trauma may be easily overlooked when it is blunt and does not cause any skin or bone lesion, as in the present instance. In the literature there is only one other detailed report[2] in which a blow on the chest did not cause skin or bone injuries and yet led to constrictive pericarditis.

CASE REPORT

J. R., a forty-two year old man, was admitted to Metropolitan Hospital on February 27, 1958, because of severe congestive heart failure. Except for an appendectomy at the age of thirty-five he had been in good health until his present illness. He had served two years in the Navy and four years as a merchant seaman.

On May 18, 1956, a wooden case weighing about 250 pounds and falling a distance of about 12 feet struck him on the anterior part of the chest. He continued to work. Two days later he noted increasing chest pain and consulted his physician. On May 22 an x-ray film of the chest showed the cardiac shadow to be markedly enlarged to the right and left. An electrocardiogram on May 23 was normal. Even in retrospect, one cannot discern any evidence of pericarditis therein, although the T waves are slightly abnormal in V_1 to V_3. It is not clear why, but there was no further investigation at this time. The pain subsided and the patient continued to work.

Four months later he noted that he blacked out momentarily whenever he lifted a heavy box over his head. Also, for the first time dyspnea and chest pain after excitement and exertion appeared. The symptoms gradually worsened so that by July 1957, fourteen months after the accident, he was forced to stop working. Early in February 1958 edema of the legs and swelling of the abdomen appeared. He was hospitalized in severe congestive failure on February 27, 1958, twenty-two months after the accident.

Physical examination showed a well developed man who was dyspneic at test. The lips and nails were mildly cyanotic; the cervical veins were prominently distended. The pulse was 76 and irregular; the blood pressure 130/110 mm. Hg. The temperature was normal. Precordial palpation could not detect any heart action. Percussion gave a marked flatness from two fingerbreadths to the right of the sternum to the left anterior axillary line. The heart sounds were distant and muffled. The posterior bases of the lungs showed a flat percussion note and diminished breath sounds. Above this region moist rales were heard. The abdomen was distended and dependent dullness and a fluid wave were noted. The liver was balloted about one handbreadth below the costal margin and was tender. Pitting edema extended from the feet to the lower thighs.

Significant laboratory findings included a trace of albumin in the urine and normal erythrocyte sedimentation rate (5 mm. per hour). Serum albumin was 3.9 and globulin 2.4 gm. per cent; alkaline phosphatase was 4.3 Bodansky units; cephalin flocculation was 2 plus in twenty-four hours. Examination of the sputums, gastric washings and the various aspirates were negative for tuberculosis and malignancy. The Mantoux tuberculin test was positive at a 1:1000 dilution.

X-ray examination of the chest (Fig. 1) showed the cardiac shadow to be greatly enlarged to the right and left. Obscuration of the right costophrenic angle with diffuse clouding of both lung fields indicated a bilateral pleural effusion. Fluoroscopy showed very small excursions of the cardiac borders.

The electrocardiogram showed abnormally low voltage in the limb and chest leads. There was a low, positive T wave in leads I and V_1 through V_6; it was negative in aVF. The S-T segment varied from a slight elevation to a slight depression in leads I, aVF, V_5, and V_6. There was also a mild respiratory variability of the QRS in lead I. The low voltage and flat ST-T complexes were consistent with pericardial disease. Subsequent records continued to show flat T waves in all leads (Fig. 2).

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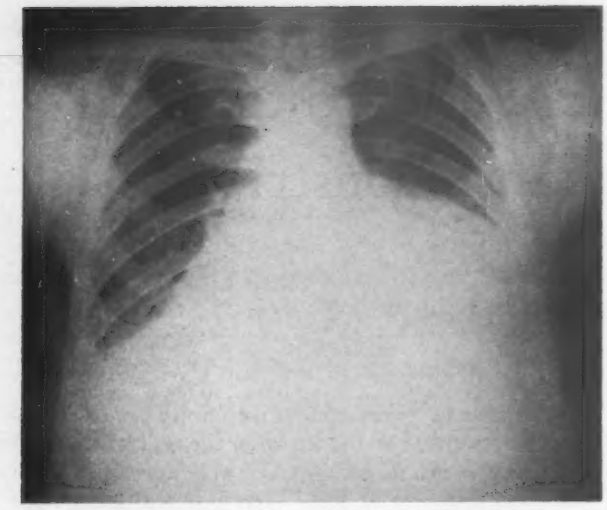

FIG. 1. Posteroanterior view of chest on March 1 shortly after admission. The cardiac shadow is markedly enlarged with bilateral pleural effusion.

Results of Pericardiocentesis: After the initial examination a diagnosis of pericardial effusion and tamponade of undetermined etiology was made. On March 3, a left pleural tap yielded 350 ml. of a dark yellow fluid with a total protein content of 1.6 gm. per cent and a specific gravity of 1.010. On March 4 a pericardial tap was attempted, using the needle and plastic catheter technic described elsewhere.[3,4] The point of insertion was in the fourth intercostal space just medial to the mid-clavicular line; 250 ml. of a thin chocolate-colored fluid were aspirated. The operator felt the needle grate on the underlying tissue, suggestive of a calcified pericardium. The electrocardiographic monitor using the needle as the exploring electrode showed a few auricular and ventricular extrasystoles. These did not have the characteristic QS form which would have resulted had the needle been the stimulus for the ectopic beats,[4] nor were there any S-T changes. Thus, the electrocardiogram failed to show any evidence of contact of the needle

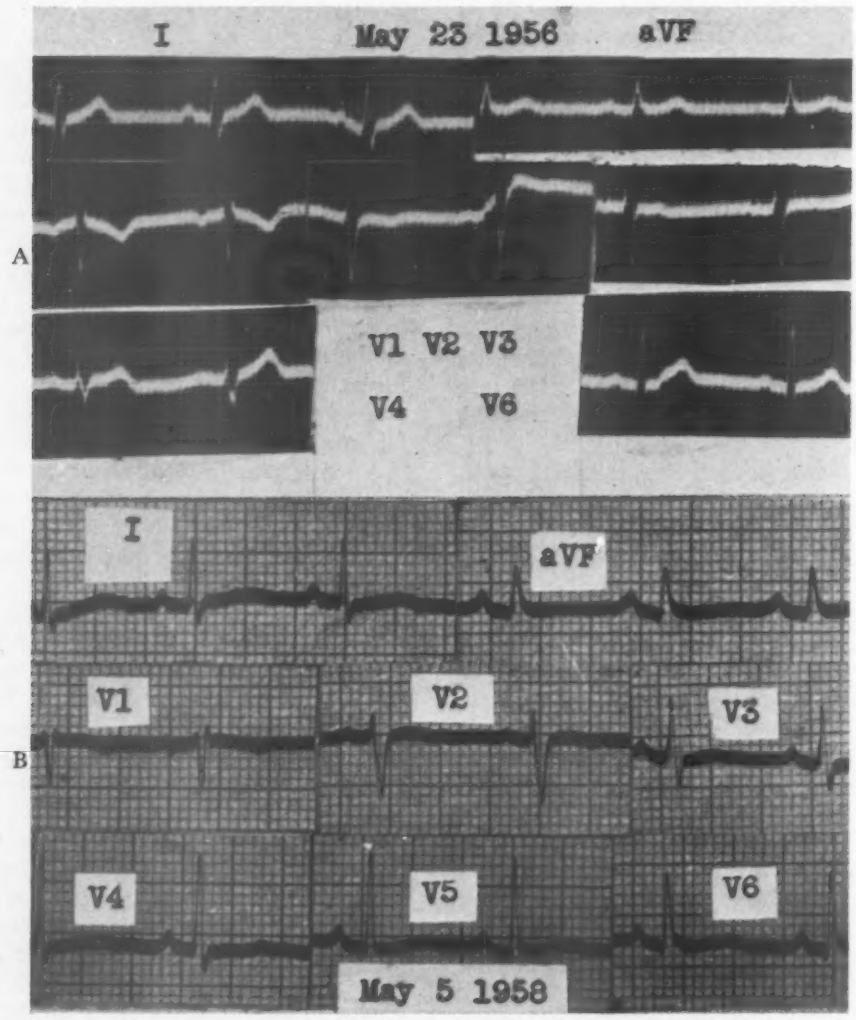

FIG. 2. The upper tracing taken five days after injury shows no evidence of pericardial or other type of abnormality. The lower tracing taken just before surgery shows the elevated S-T and flat T characteristic of pericardial disease.

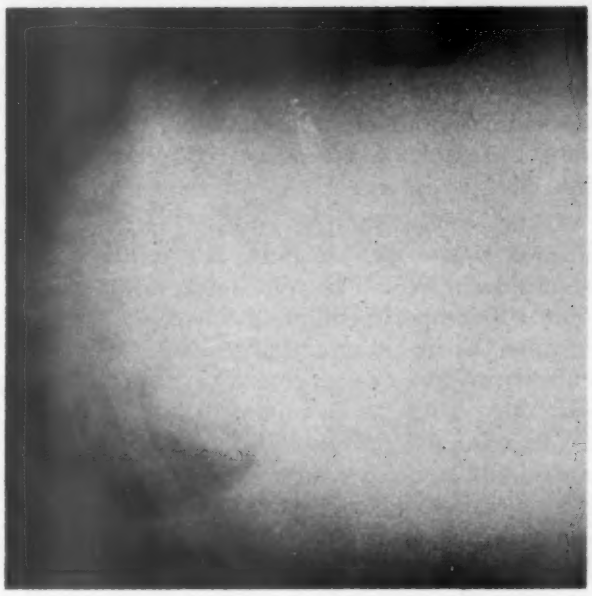

FIG. 3. Anteroposterior view with patient lying on right side with left side up. Taken immediately after the first "pericardial" tap. Note the air and fluid levels outlining the pleural loculations.

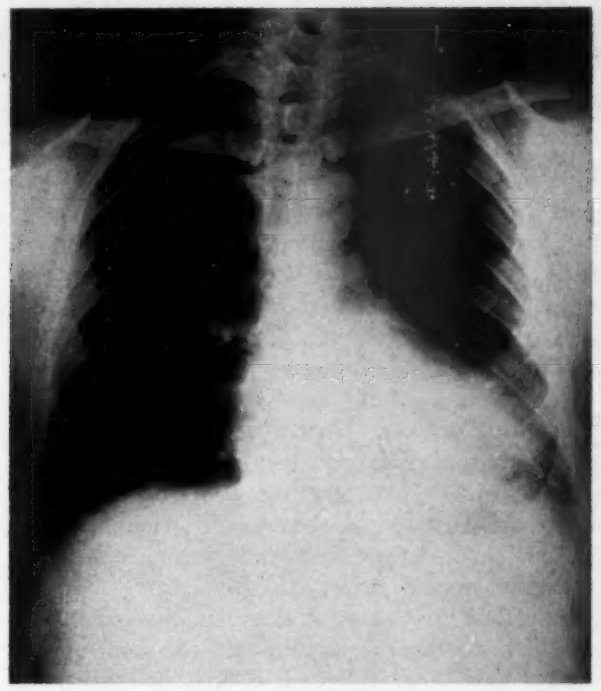

FIG. 4. Seven months after pericardiotomy. The enlargement of the cardiac shadow to the left is probably the expression of pleuropericardial thickening.

with the myocardium as would have occurred had the needle either indented the pericardium or pierced it. Two hundred milliliters of air were injected through the catheter after obtaining the fluid. X-ray examination in various postures showed air and fluid levels in extracardiac pleural loculations (Fig. 3). There was no air visible in the pericardial sac. Thus, both the electrocardiographic and x-ray findings indicated that the pericardial sac had not been entered.

On March 11 and March 27, two more precordial pericardial taps were attempted; they yielded 300 and 450 ml., respectively, of the same type of brown fluid. Again, grating of the needle was noted. Again, the injected air did not lie in the pericardial sac but in left pleural loculations. On March 21 and March 26, left pleural taps yielded 1,500 and 750 ml. of blood-tinged fluid, respectively.

Clinical Course: The patient did not show any substantial improvement after any of these taps. On March 28, the venous pressure measured 250 mm. of saline and the arm-to-tongue circulation time using sodium succinate was twenty-seven seconds.

At the time of the first "pericardial" tap, when it was thought that the aspirate originated from the pericardial sac, the diagnosis of a traumatic hemopericardium was considered because the chocolate-colored fluid suggested an old hematoma. At this time questioning elicited the history of trauma to the chest. When it was evident that the hematomas drained lay near but outside the pericardial sac, the diagnosis was changed to constrictive pericarditis with juxtacardiac pleural hematomas caused by injury.

The congestive failure persisted in spite of the multiple taps, bedrest, and administration of digitalis and diuretics. A trial of antituberculous therapy for four weeks also failed to improve the patient's condition.

Operative Findings and Results: On April 23, 1958, he was transferred to the Thoracic Surgical Service. On that day 750 ml. of straw-colored fluid were aspirated from the right pleural cavity and 1,500 ml. of blood-tinged fluid from the left pleural cavity. An operation was performed on May 5.

The left pleural cavity was entered through the fourth intercostal space anteriorly. The enlarged pericardial sac bulged into the wound. A small opening was made and about 800 ml. of a thin brown fluid were evacuated. On opening the pericardium further, no evidence of adhesive pericarditis was found. The surface of the heart was firmer than usual with increased vascularity. Two pieces of parietal pericardium 3 by 4 and 2 by 3 inches large on each side of the left phrenic nerve were excised. The parietal layer was thickened and roughened on its inner surface. Microscopic examination showed an organizing clot and desquamated mesothelial cells.

After an uneventful postoperative course the patient was discharged seventeen days later. By then all signs of congestive failure had disappeared. At present, July 1959, he has regained almost all his strength. He no longer has any dyspnea even after climbing several flights of stairs. He is working at a moderately strenuous task as an operator of a metal punch machine. His electrocardiogram has returned to normal with regard to both the voltage and S-T changes. The teleoroentgenogram eight months

postoperatively showed marked reduction in heart size (Fig. 4).

Comments

No mention was made by the surgeon of any loculated hematoma around the heart which had been diagnosed preoperatively from the x-ray examinations made after the injection of air. It is possible that the multiple chest taps done just prior to surgery had emptied and collapsed them.

The grating of the needle noted in the course of the "pericardial" taps suggested some calcification of the pericardium. Neither the x-ray examination nor the surgeon found the calcification. The grating probably resulted from the contact of the needle with a hard, fibrous pericardium. In retrospect, it is clear that the needle never did penetrate into the pericardial sac. Had it done so, the old blood would have been aspirated and the tamponade would have been relieved, at least temporarily.

A hemopericardium is an essential phase in the development of a traumatic constrictive pericarditis. It has been reported that nonpenetrating trauma may induce a peri- and epicarditis; however, it is unlikely that it alone can lead to a significant fibrosis and constriction. Hemorrhage into the pericardial sac is common after diagnostic needling of the heart,[6,7] and it is not rare in myocardial infarction, especially in the presence of anticoagulants. Yet, the subsequent development of constrictive pericarditis is most unusual, for the blood is resorbed before any significant fibrosis develops. It is not clear why, as in the present case, constrictive fibrosis occasionally ensues.

The absorption of blood from the serous cavities is reviewed by Courtice and Simmonds.[9] For the cells and plasma proteins it occurs almost exclusively by way of the lymphatics. The pericardium absorbs blood much more slowly than either the peritoneum or the pleura. During its stay in the pericardial sac, the blood may irritate the lining. Ehrenhaft and associates[2] found that in dogs the intrapericardial instillation of the lipid fraction of blood caused pericarditis which in some instances resulted in fibrosis, calcification, and even constriction. Other blood fractions did not irritate the lining significantly.

Blood in the sac usually deposits its fibrin on the lining; occasionally it forms a clot within the lumen. It may be assumed that this is followed by two opposing processes: fibrinolysis and organization. Fibrinolysis tends to dissolve the clot. The liquid blood then may remain unabsorbed for years, as in the present case. Organization tends to convert the clot into fibrous tissue.

If the blood is completely absorbed and if the fibrous tissue formed does not contain any hemosiderin, it will be impossible to determine that a hemopericardium initiated the process from a tissue examination alone. This occurred in a case of constrictive pericarditis resulting from a hemopericardium after a myocardial infarction.[8] Presumably it could also occur in a case of traumatic hemopericardium. In such a case it would be impossible to diagnose the traumatic etiology, unless the antecedent events were known. Therefore, instead of assigning a tuberculous etiology to every cryptogenic case of constrictive pericarditis, one should consider the possibility of trauma or other cause of hemopericardium.

One gains the impression from the literature that the amount of blood in the sac influences the outcome. When small, the ensuing fibrosis is usually insignificant. Only when the amount is large, and even then not always, does troublesome fibrosis and constriction develop. These considerations suggest the following therapeutic plan, given a case in which the clinical picture indicates a hemopericardium: If the size of the heart does not increase much, then the diagnosis of hemopericardium is no indication for active therapy. If the heart size increases greatly, one should reduce the hemopericardium by needle and catheter drainage, even in the absence of tamponade.

Inasmuch as constriction may develop in spite of an early aspiration,[3,8] the patient must be watched for several years to detect such a complication early. During the so-called free interval between the original insult and the constrictive phase, there are enough signs to make a diagnosis and institute therapy early, provided the patient is under competent medical observation. Either x-ray or electrocardiogram abnormalities, or both, can be expected in the free interval. If the treatment is early, the scar is more amenable to resection and the myocardium has not suffered compression and disuse atrophy. I have not yet found a single instance in which adequate observation failed to disclose evidence of a continuing process in the course of a developing constrictive pericarditis.

Summary

A blunt injury to the chest wall caused a loculated hemothorax and hemopericardium. This led within two years to cardiac tamponade and constrictive pericarditis, with persistence of old degenerated blood in the pleural and pericardial cavities. Pericardiotomy with removal of the old blood and excision of a small piece of parietal pericardium has relieved the constriction and restored the patient to complete health.

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Diagnostic Shelf

Effect of Respiration on the Pericardial Friction Rub*

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A PERICARDIAL FRICTION rub is the earliest and most dependable sign of pericarditis. Its intensity is determined by various factors: (1) contact of the parietal and visceral sheets of the pericardium; (2) character of the exudate, either thin, fibrinous or coarse, or shaggy deposits; (3) force of cardiac contraction; (4) distance of the site of auscultation from the rubbing surfaces.

Effect of Inspiration on Intensity of Friction Rub: Most modern texts make no mention of the effect of respiration on the pericardial friction rub. Where this point is discussed, the conventional view is expressed that the pericardial rub, like endocardial murmurs, becomes louder during expiration.[1,2] My own observations lead to different conclusions. Thirty-nine cases of pericarditis in which a pericardial friction rub was audible were observed in the past three years. In twenty-six instances I was able to follow closely the clinical course and to listen to the heart almost every day. In nine cases I noticed with some surprise that the pericardial rub was either louder or audible only in the inspiratory phase. These findings were confirmed by other observers. In one instance the rub was initially heard in both phases of respiration. When, however, signs of accumulation of pericardial fluid appeared, the rub became audible only during the inspiratory phase. In no instance, however, had expiration a significant influence on the loudness of the pericardial friction rub.

Study of older German and French cardiac texts[3,4] reveals that the effect of inspiration upon the pericardial friction rub, as observed in our study, was known more than half a century ago. Potain[5] pointed out as early as 1887 that the pericardial rub is loudest during inspiration, because it is then that the roughened surfaces make the greatest excursions.

Causes of Loudness of Friction Rub During Inspiration: Since during inspiration the expanding lungs cover the front of the heart, thus diminishing the intensity of cardiac sounds, obviously other factors are simultaneously called into play which produce the effect upon the pericardial rub mentioned previously. One factor is *increased filling of the heart;* another resulting from the former is *greater force of cardiac contraction.* A third factor seems to be *inspiratory descent of the diaphragm.* The pericardium is fixed caudally to the centrum tendineum of the diaphragm and cranially to the great vessels (Fig. 1A). Its anterior portion covers the convex surface of the outflow tract of the right ventricle in the sternal area where a pericardial rub is heard most often. When the diaphragm descends and the cranial point of the pericardial fixation does not move to the same extent, stretching of the convex pericardium results (Fig. 1B). This causes closer contact of the two pericardial sheets even when they were separated in the expiratory phase by a thin layer of fluid which may be displaced laterally or toward the bottom of the pericardial sac. The simultaneous effects of increased filling of the heart, greater force of cardiac contraction and stretching of the pericardium result in intensification of the pericardial friction rub during the inspiratory phase. In my experience this effect becomes manifest with ordinary rather

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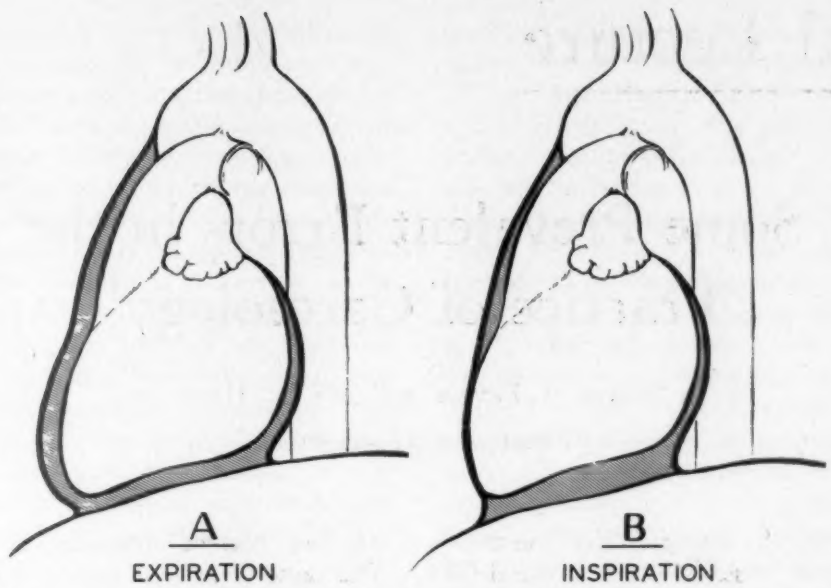

FIG. 1. A, expiration; the heart and great vessels are seen in the left lateral view during expiration. The anterior portion of the pericardium descends in a convex line from its point of fixation at the great arteries to the diaphragm. A small layer of fluid fills the pericardial sac. B, inspiration; during inspiration the pericardium is stretched by the descent of the diaphragm and contacts the epicardial surface, displacing the fluid from the anterior aspect to the bottom of the pericardium.

than exaggerated inspiration. However, when the two sheets of the pericardium are already in close contact during expiration, no further intensification of the rub occurs in the inspiratory phase.

Differentiation from Pleuropericardial Rub: The finding of increased loudness of the pericardial rub during the inspiratory phase in two cases of our study led skilled observers to the erroneous diagnosis of a pleuropericardial rub. In both instances the friction rub followed strictly the rhythm of the heart beat and could not be heard beyond the limits of the sternum and its immediate neighborhood. Nor could a rub of pleural character, that is, synchronous with the phases of respiration, be elicited on deep respiration, either over the precordium or over other portions of the chest. The presence of a pericardial effusion was ascertained in these cases both by percussion and serial x-ray studies. It is well known that accumulation of even a large quantity of fluid in the pericardial cavity is compatible with the finding of a pericardial friction rub.[6] This, of course, presupposes that the anterior portion of the pericardial sac contains either no fluid or only a thin layer which can be displaced during inspiration by the forces mentioned above.

SUMMARY

A study of twenty-six cases of pericarditis displaying a pericardial friction rub was made. In nine instances the pericardial rub became either louder or was audible only in the phase of inspiration. The factors which may account for this finding are increased filling and force of cardiac contraction and stretching of the pericardium due to descent of the diaphragm in the inspiratory phase.

A pericardial rub which is louder during inspiration should not be mistaken for a pleuropericardial rub.

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Special Lecture

Some Prevalent Errors in the Practice of Cardiology*

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A FEW DECADES AGO it seemed that the treatment of heart disease was at a standstill. What was more depressing was that the immediate prospects seemed gloomy. Very little hope was felt concerning the prevention or effective treatment of hypertensive heart disease, coronary artery disease or valvular heart disease. The diagnosis of the various types of heart disease had already become quite accurate, but there generally was very little reward to the learned physician who made a correct though difficult diagnosis. At present the situation is quite different. The advances in modern cardiac surgery have been so great and there has been so much improvement in the medical management of cardiac disease that many conditions which were previously hopeless can now be cured or greatly helped. With these advances in knowledge it becomes more and more imperative that the physician remain alert and not overlook those conditions that can be helped. Errors are often no longer purely academic. With the greater availability of effective treatment for previously incurable conditions, the responsibility of the physician increases. The purpose of this discussion is to take up some of the important errors in the care of cardiac patients. They include errors that I know I have made and that I see occurring in general practice.

ERRORS IN DIAGNOSIS

Of greatest importance are errors in diagnosis. It is obvious that in many instances treatment will be ineffective or not altered whether correct diagnosis is made or not. The same treatment will be outlined for heart failure, if present, whether the cause were amyloid disease, endocardial fibroelastosis, Fiedler's myocarditis, scleroderma heart or many other incurable types of heart disease. It would matter little if these conditions were overlooked. However, there are still many curable conditions that are missed. These deserve particular emphasis.

THYROID HEART DISEASE

Hyperthyroidism: Masked thyrocardiac disease frequently goes undetected. This is particularly true if some other type of heart disease, is also present such as coronary, hypertensive or rheumatic valvular disease. Such patients are treated for what they obviously have, e.g., mitral stenosis or hypertension, but the hidden thyrotoxic state remains uncontrolled and prevents improvement from taking place. Because of the absence of exophthalmos or an obvious goiter one is dependent on important but less distinctive clinical clues. Among them are a faint stare to the eyes (sometimes unilateral), a slight tremor of the fingers, an excessive appetite, hyperactive bowels, undue loss of weight, preference for cold weather, early graying of the hair and a warm, hyperemic, somewhat pigmented or salmon-colored face. Of particular importance is unexplained transient or even permanent auricular fibrillation and the failure of the grossly irregular ventricular rate to slow adequately on full digitalis therapy. When this possibility arises,

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it must be realized that when the thyroid gland cannot be felt it might yet be found on x-ray examination in the upper mediastinum or by the detection of a calcified nodule or a deviated trachea. Reliable laboratory tests are now available to confirm or eliminate the diagnosis of hyperthyroidism, once it is considered. What is most important is that the response to therapy, whether it is medical or surgical, is very satisfactory and often dramatic.

As stated previously, patients with masked thyrocardiac disease often have other independent forms of heart disease. It has not been generally appreciated that a hyperactive thyroid gland of itself can occasionally be the sole cause of advanced congestive heart failure that would be entirely reversible if the thyrotoxicosis were cured.

Myxedema: The opposite error is much rarer but also of importance, i.e., overlooking *myxedema heart disease.* Here the diagnosis is not difficult once it is thought of and treatment is simple and effective and the results often dramatic. With the use of tests such as the radioactive iodine uptake, protein-bound iodine, basal metabolism and blood cholesterol it should not be difficult to establish the correct diagnosis. It should be thought of in any case in which there appears to be unexplained dilatation of the heart. In most such cases the so-called "dilatation" in fact proves to be a true hydropericardium. What is not generally known is that on very rare occasions ascites, requiring repeated abdominal tappings, may also occur with myxedema and may vanish with appropriate thyroid therapy. I recently had an experience of this sort in which the presumptive diagnosis had been cirrhosis of the liver, neoplasm of the abdomen or congestive failure from myocardial disease. The finding of a normal venous pressure made it very unlikely that the dilated cardiac silhouette on x-ray examination and the ascites could be explained on the basis of congestive heart failure. Then the radioactive iodine uptake test proved to be only 1 per cent. This fairly well established the diagnosis of myxedema. The patient has been quite well for two years since he was given thyroid tablets orally.

PERICARDIAL CONSTRICTION

Another uncommon condition that is frequently overlooked is *constrictive pericarditis.* When it occurs in older individuals, especially males, it is likely to be regarded as coronary artery disease. When a man over fifty years of age has atypical chest discomfort, some shortness of breath and shows very little on physical examination of the heart except for possibly some cardiac hypertrophy and a slight systolic murmur, he is apt to be diagnosed as suffering from arteriosclerotic heart disease. The diagnosis gains further support when the electrocardiogram report reads that the tracings are consistent with coronary heart disease, because of some flattening or inversion of the T waves. The difficulty is that any type of electrocardiogram is consistent with coronary sclerosis, even perfectly normal tracings. A few simple clinical findings may serve to direct attention to the correct diagnosis. If the patient has markedly distended cervical veins with a venous pressure of over 250 mm. Hg, yet can lie flat fairly comfortably and especially if a definite third heart sound is heard at the apex (a so-called diastolic rebound), the most probable diagnosis is pericardial constriction. Such patients may also develop a striking suffused appearance to the face and neck immediately on lying down which is not present in the upright position. When some of these clinical features are detected, one should search carefully for x-ray evidence of pericardial calcification and other evidence of pericardial disease. Even an exploratory operation would be justified when the diagnosis is doubtful, because the therapeutic result may be remarkable and the surgical risk is very slight.

One clinical aspect of pericardial constriction that only recently has been appreciated is that it may result from *trauma.* Accidents, especially a steering wheel blow to the chest, that cause hemorrhage into the pericardial sac may end up with calcification. In fact, if a significant amount of blood remains undetected in the pericardial cavity, it can be the forerunner of pericardial calcification. The two possible causes for otherwise unexplained cases of pericardial constriction with or without calcification are previous trauma to the chest or some form of cardiac surgery. I have already seen two instances that followed years after an accident and one that developed some months after an operation on the aortic valve. Another cause of pericardial constriction that only now has become identified is so-called benign or virus pericarditis. Rarely does this lead to constriction.

CORONARY ARTERY DISEASE

Angina Pectoris: Errors in the diagnosis of angina pectoris are not very costly because at the present time there is no satisfactory effective method of cure of the condition. In general it would seem that less harm is done to the patient if the physician overlooks angina or regards a certain discomfort in the chest as benign and makes light of it when it proves to be truly anginal in character, than when he does the reverse and calls the condition angina when no organic heart disease at all is present. In the first instance the patient is likely to slow up or stop when the signal of distress appears. His symptoms are a good guide for his activities. When the second type of error is made, the patient's life is often made miserable. A constant fear of sudden death develops and he may lead a markedly restricted and unhappy life unnecessarily. These errors in judgment are common, despite the fact that the correct diagnosis of angina pectoris can be made in the overwhelming majority of cases.

One simple new test, in addition to all the other means available, is the so-called "carotid sinus test." This may be helpful for, when positive, it is practically specific. If the physician observes the patient while having a spontaneous spell of chest discomfort, he should immediately massage the carotid sinus for only several seconds, with the patient sitting up preferably. If there has been moderate or marked slowing of the heart, the physician promptly asks whether the pain or discomfort was made *worse*. It is most important to ask a misleading question. The patient is likely to pause for a second, appear to look into his chest and then reply, "No, the pain is gone, or "No, it is letting up." If one obtains such a reply, one can be fairly certain that the pain was anginal. Relief comes in seconds, not in minutes; and it comes even when the question put to the patient might readily have misled him. If no slowing is produced by the carotid sinus massage, no conclusion can be drawn. If good slowing is obtained but there is no relief, the discomfort was most likely not anginal. It could be due to a coronary thrombosis, although even in some of these the pain is lightened for some seconds. The carotid sinus test has proved very helpful in many otherwise puzzling cases.

Although in angina the most common circumstance which precipitates the pain or distress is walking in the street, especially up hill or in cold air or after a meal, there are numerous exceptions. These cases may be difficult to diagnose. I recall some errors I have made in the past when repeated spells of chest pain were entirely unrelated to physical effort and physical examination was completely negative. I would then mistakingly regard the heart as normal only to learn thereafter that the patient had an overt coronary thrombosis or more classical anginal symptoms developed. There are instances in which the pain comes at rest, in bed, on emotional upsets or without any known cause and yet the patient is able to walk in the street even briskly. At other times a patient may be able to do very strenuous work indoors and yet not be able to walk one block out of doors. In a word, foot pounds of work do not seem to be the sole determining factor in precipitating anginal pain. In such cases all means should be employed that might help in the diagnosis, including the response to nitroglycerine, a Master two-step test, if possible the carotid sinus test just described and direct observation during an actual episode.

Errors in Electrocardiographic Diagnosis: One could elaborate at great length concerning the large number of abnormalities in the electrocardiograms that are incorrectly interpreted as indicative of coronary artery disease. It is particularly worthy of emphasis that right bundle branch block, complete or incomplete, although frequently seen with coronary, valvular and congenital heart disease, is also met with frequently in patients with little or no other evidence of organic heart disease. Such individuals may be able to lead a perfectly normal life. Likewise, there are patients who are diagnosed as having coronary disease because the electrocardiograms show a persistent well marked elevation of the S-T segment in some of the conventional limb leads or in the precordial leads. These tracings do not look like those seen with acute myocardial infarction or ventricular aneurysm and can be found in patients with perfectly normal hearts.

Coronary Disease Associated with Noncardiac Causes of Chest Pain: A common difficulty when the question of angina arises is the finding of a *hiatus hernia*, *gallstones*, *peptic ulcer* or *spinal arthritis* during the complete survey of the case. Not infrequently the discomfort or pain in the chest is ascribed to one of these other conditions because there is objective evidence for that diagnosis and no abnormal physical findings in the heart itself. Inasmuch as these other

noncardiac conditions are very common, it should not be surprising that one or more of them would be met with among the hundreds of thousands of cases of coronary artery disease in this country. I have seen instances in which all four of the above mentioned diseases were present in addition to classical angina. There are very large numbers of patients with coronary disease who also have gallstones, peptic ulcer, hiatus hernia or spinal arthritis or combinations of these conditions. A very common error is to confuse hiatus hernia or gallstones with angina. If the history is classical for angina pectoris or if one of the tests discussed previously, especially the carotid sinus test, is positive, one must say that the patient has angina in addition to hiatus hernia or gallstones. Too often the primary complaints are ascribed to an innocent symptomless hiatus hernia or to the gallbladder when they are entirely due to the heart. Much less often the reverse error is made. When the pain is lessened or relieved by rising from a recumbent to an upright position, it is too frequently regarded as further evidence of hiatus hernia. This relief of pain on sitting up is even more characteristic of angina pectoris than it is of hiatus hernia.

Some of the above deductions would have to follow from a purely statistical point of view. Although the following figures are not absolutely accurate, they probably are not far from the truth and will in any event illustrate the principle involved. There may be about 3,000,000 individuals in this country with clinical coronary artery disease. Very likely 10 per cent of these (300,000) have or have had gallstones as well. Ten per cent of these (30,000) probably also have hiatus hernia. Furthermore, 10 per cent of the latter have a peptic ulcer (3,000) and 10 per cent of latter (300) also have spinal arthritis. This is not merely an arithmetical juggling of figures. I am fairly certain that they are an understatement rather than an overestimation of the facts and that there are more than 300 individuals who have all five of the conditions when the primary problem is coronary artery pain.

MYOCARDIAL INFARCTION

Acute Dissection of the Aorta: The distinction between an acute coronary episode and an acute dissection of the aorta is frequently difficult. The question is no longer merely academic as some patients with aortic dissection are now being operated upon with success. One should keep this possibility in mind particularly when there is moderate or severe chest distress that does not radiate to the arms and is not accompanied by shock, arrhythmias, electrocardiographic changes or fall in blood pressure, but when the x-ray film may show gradual enlargement of the aortic shadow during the early few days following the onset of the illness. One very peculiar and rather characteristic type of pain that comes in some cases of aortic dissection is a sudden severe pain in the back of the center of the mouth. I am not aware that this occurs with coronary artery disease. It must be borne in mind that there is overlapping of the above findings in the two conditions so that, for example, there often is no radiation of pain into the arms in a coronary attack and there may be some fall in pressure with a dissection of the aorta.

Acute Benign Pericarditis: A more common difficulty is distinguishing acute benign pericarditis from acute myocardial infarction with pericarditis. The age may be helpful in that simple pericarditis is not infrequent in younger individuals. One valuable feature is that left pleuritis with effusion is common with acute benign pericarditis and rare with a coronary attack. In the latter condition when pleural fluid is present, it is much more likely to be found on the right. Also pericardial fluid sufficiently marked to be recognized by an increase in the cardiac silhouette on x-ray examination is very rare in myocardial infarction and common with simple pericarditis. The pain in pericarditis is often accentuated on deep breathing or on movements of the chest and trunk. Furthermore, although there are changes in the T waves and the S-T segment of the electrocardiogram in both conditions, they are not quite the same and Q waves rarely, if ever, develop as a result of benign pericarditis.

DYSPNEA

The assumption that an individual who is short of breath has heart trouble is made too readily. Although the most common cause of troublesome breathlessness is organic cardiac disease, there are many other causes, some of which are essentially benign. Before concluding that a patient's dyspnea is due to heart disease it is first well to find satisfactory evidence that the heart is structurally diseased. Even when this evidence is quite clear, it is important to try to estimate how much of the dyspnea may be due to other more benign causes. In so far as

these other noncardiac factors are involved, the condition may be much less serious than appears at the outset. The presence of anemia, obesity, emphysema, general fatigue and anxiety all may contribute appreciably in the production of dyspnea. In some instances dyspnea from these latter conditions is superimposed on true cardiac failure. In others, although organic heart disease is present, the major complaint of breathlessness is entirely due to these noncardiac causes and the heart is actually well compensated. In a third group the physician makes the error of thinking that there is heart failure when the heart is quite normal and the symptoms are entirely due to an anxiety state, obesity or emphysema.

Functional Dyspnea: A few simple clinical points often help to avoid these errors. Patients with functional dyspnea often have "sighing breathing" or "air hunger" which does not occur with true heart failure. These patients are generally short of breath at rest and while sitting upright. When an organic cardiac is sick enough to be breathless at rest, he is obviously quite ill and simple physical examination will quickly confirm the diagnosis. Furthermore, patients with functional cardiac disease practically never have paroxysmal nocturnal dyspnea. When a patient is awakened from sleep breathless, has to sit up with his feet hanging over the side of the bed, has a cough and a wheeze and obtains relief not in a second or two but in fifteen minutes or so, one can be fairly sure he has important organic heart disease. In doubtful cases the finding of a normal-sized heart and a normal vital capacity of the lungs helps to assure the physician that the heart is normal or well compensated.

Anemia: The general feeling of weakness that is associated with significant anemia or with any condition in which the entire body is asthenic may be responsible for the feeling of breathlessness. It is as if the burden of deeper and more rapid respiration on effort is tiresome. It is obvious that digitalis will not help this condition.

Dyspnea of Pulmonary Origin: A more difficult problem that often causes confusion is one that results from mistaking dyspnea due to *bronchial disease* or *emphysema* with that due to heart failure. Although both mechanisms may be present in the same individual there are many patients who are quite short of breath who receive meticulous treatment for heart failure, including full doses of digitalis, when the heart is perfectly normal and the breathlessness is entirely due to emphysema. When a patient complains of shortness of breath, especially if he is over fifty years of age, the physician immediately thinks of heart disease. The presence of râles in the chest fortifies this suspicion. If other findings are detected, such as hypertension, a slight cardiac murmur or some nondiagnostic changes in the ventricular complex of the electrocardiogram, the physician becomes convinced that the heart is the cause of the dyspnea. Under these circumstances the patient continues to do poorly and in fact may deteriorate. When a cardiac's progress is not favorable, the digitalis dosage may be increased to the maximum. In general, it is true that when full doses of digitalis are given to one whose heart is not diseased or failing, the situation is worsened. In addition to the continued dyspnea the patient may lose weight and strength because of the anorexia and general ill feeling brought on by digitalis.

Such errors can be avoided by some simple clinical observations. The râles in the lungs when due to emphysema are squeaky, sibilant or very coarse, both inspiratory and expiratory, and are often heard in the front as well as the back of the chest. Those of congestive failure are generally heard at the bases of the lungs and, when present anteriorly, the patient is likely to be quite ill or have acute pulmonary edema or pulmonary infarction. Dyspnea from emphysema is rarely of the paroxysmal nocturnal type and, in fact, is not present at rest except in the very severe stages. The x-ray finding in the chest are most helpful and often decisive in distinguishing bronchial from cardiac dyspnea. The low diaphragms, hyperaerated lungs, the lack of congestion in the smaller pulmonary vessels as seen on x-ray examination and the small or normal-sized heart make the diagnosis of cardiac congestion untenable and practically establish the diagnosis of emphysema.

It must not be inferred that with emphysema there may not be right-sided heart failure. Chronic cor pulmonale is not at all rare and then digitalis and other cardiac therapy may be helpful. The point to bear in mind is that most patients who have emphysema and are short of breath have no heart failure for long periods of time, many years in fact. During that time digitalis will do no good and bronchial dilators containing preparations like isoproterenal, ephedrin, aminophyllin, may be of considerable value. One of the most helpful clues to guide

the physician in problems of this sort is that if the heart is found to be smaller than normal or normal in size, it is extremely unlikely that heart failure is present or that digitalis will do anything but harm. The only exception to this general rule is the presence of a rapid ventricular rate due to an arrhythmia like atrial fibrillation or some form of tachycardia that drugs like digitalis, quinidine or procaine amide might control. I have seen numerous instances, especially among elderly individuals, in which the entire course of the illness was changed for the better by omitting all digitalis and administering preparations like isoproterenal or ephedrin. They were patients who were breathless from slight to moderate emphysema but had been regarded even by cardiologists as suffering from cardiac failure. The first hint that the diagnosis was wrong often came from finding a normal or small-sized heart. Then the study of the circulatory dynamics and the x-ray examination of the chest confirmed the original impression. Such patients are very grateful for the change in treatment and the brighter outlook that results.

CARDIAC ARRHYTHMIAS

Atrial Fibrillation: The finding of atrial fibrillation, either transient or permanent, is too readily regarded as indisputable evidence of organic heart disease. Although it is very commonly associated with rheumatic valvular disease (especially mitral stenosis), hypertensive heart disease or myocardial disease with or without coronary sclerosis, there is a significant group in which it is found with no detectable heart disease or as a result of disease of the thyroid gland. If the three above mentioned etiologic factors of heart disease can be eliminated, careful search for hyperthyroidism should first be carried out. If this is entirely negative, serious consideration should be given to the possibility that the atrial fibrillation was originally a benign arrhythmia. Atrial fibrillation may be annoying but generally by itself does not produce gross heart failure. I am certain, however, that if uncontrolled and if it lasts long enough, cardiac enlargement and congestive failure can result. Even at this more advanced and neglected stage, the condition may be entirely reversible if a normal rhythm can be established following quinidine therapy. I have seen the heart return to normal size and all dynamic measurements of the circulation become normal and remain so for many years after regularization of the rhythm. These cases form a small but rewarding group in which chronic heart failure may be truly curable.

There are additional comments that are pertinent in this discussion. I believe that in some of these cases of atrial fibrillation when the laboratory evidence of hyperthyroidism is slight or doubtful, thyrotoxicosis may yet be present. It is obvious that if the basal metabolism had been −20 per cent originally while a patient was well and he then gradually developed a mild hyperthyroid state, he could be seen later with a metabolism of only +5 per cent and yet be definitely thyrotoxic. If a definite adenoma can be found on palpation of the gland or on x-ray examination or if stigmata of thyrotoxicosis can be detected clinically or by means of the radioactive iodine test, the patient should be treated medically or surgically for hyperthyroidism. Some stubborn cases of paroxysmal atrial fibrillation in this way may be helped or cured. The second point is that the thyrotoxic state may be an additional factor, often overlooked, when obvious mitral, hypertensive or coronary disease is also present. Finally, it is not unlikely that some cases of chronic myocarditis or nonvalvular heart disease of undetermined origin with atrial fibrillation may have started as instances of masked thyrotoxic heart disease or as cases of atrial fibrillation without any important disease and in the course of time reached the irreversible stage. The inference from the foregoing is that attempts to re-establish a normal rhythm when atrial fibrillation persists should be made more frequently in cases of nonvalvular heart disease.

Diagnosis: Difficulties still prevail in the interpretation and the treatment of certain cardiac arrhythmias. This is particularly true of the various types of paroxysmal rapid heart action even after electrocardiographic tracings have been obtained. Frequently, the diagnosis remains in doubt or is actually mistaken because a tracing is not obtained during carotid sinus stimulation. This simple maneuver may readily establish the diagnosis of atrial flutter when otherwise it is misdiagnosed as normal sinus tachycardia or paroxysmal atrial tachycardia. It also may help in establishing the diagnosis of paroxysmal atrial tachycardia with block. Inasmuch as this latter condition is generally the result of digitalis intoxication and can be controlled by potassium salts or procaine amide, and the other atrial arrhythmias

with which it is confused required further digitalis, the differentiation is of vital importance. If the atrial rate can be detected as being over 250 and especially over 300, the condition is most likely atrial flutter. When the P waves can be identified as miniature with isoelectric intervals between them in lead II and the atrial rate is between 150 and 240, it is most likely paroxysmal atrial tachycardia with block. One can readily see that with one interpretation the patient would require more digitalis (atrial flutter or fibrillation with rapid ventricular rate) while with a different interpretation (paroxysmal atrial tachycardia with block) additional digitalis might well result in a fatality.

Another difficulty is the distinction between paroxysmal ventricular tachycardia and atrial fibrillation or supraventricular tachycardia with concomitant bundle branch block. This at times is very difficult. Search should be made for P waves coming independently of the ventricular complexes, even by trying carotid massage or obtaining esophageal leads. Establishing the correct diagnosis is important because drug therapy is quite different in ventricular than in auricular tachycardia. There are other points that may help in the differentiation of arrhythmias that will not be taken up here. Suffice it to emphasize that careful study will frequently be rewarding and may occasionally make the difference between life and death.

MITRAL STENOSIS

With the advent of cardiac surgery for many forms of heart disease, the diagnosis of the exact anatomic diagnosis has become very important. In the past it mattered very little whether the diagnosis of mitral stenosis was made or not or whether the degree of stenosis was accurately appraised. Now it is often very vital to know these details. It is not the purpose in this discussion to review all the points involved in the diagnosis of valvular disease of the heart. There are a few errors, however, that are worth taking up. The first is that in auscultation of the heart the physician must concentrate his attention on one feature at a time. He must tell himself that for the next ten to twenty seconds he will listen to the diastolic interval at the apex with such intensity that having done so he will not be able to say whether a systolic murmur is present or not. He had focused his attention exclusively on diastole. In that way the faint apical diastolic rumble of mitral stenosis will not be overlooked. The same thing is true of a faint but diagnostic early basal diastolic murmur of aortic insufficiency. I have frequently made these simple but previously overlooked diagnoses not because my hearing is any more acute but because I concentrate on one part of the cardiac cycle at a time.

Absence of Diastolic Murmur: Another difficulty that now confronts us is that in certain cases of mitral stenosis there may be no audible murmur at all in diastole. This may not be misleading if the physician had observed the patient previously. It then is very probable that for years the classical diastolic or presystolic rumble was readily detected. Only in the course of time, particularly after atrial fibrillation appeared and advanced congestive failure developed, did the diastolic murmur entirely disappear. However, when a physician sees such a patient for the first time in this latter stage, he may overlook the diagnosis entirely. The condition may be regarded as chronic cor pulmonale or chronic myocarditis of undetermined origin or painless coronary sclerosis with atrial fibrillation. One should make every effort to eliminate from consideration a tight mitral stenosis which may yet be present, particularly looking for a calcified mitral valve or a prominent left atrium on fluoroscopy. When the suspicion is sufficient, it may be wise to perform left heart catheterization, looking for a gradient across the mitral valve. This problem is of considerable importance because there are instances of tight mitral stenosis with only a very inconspicuous diastolic murmur that can be helped greatly by mitral valvuloplasty.

CONGENITAL HEART DISEASE

The problems of congenital heart disease and the various operative procedures that are becoming available are so involved and changing so rapidly that the average physician, internist or even cardiologist finds himself incapable of meeting many of the situations that arise. There is no difficulty in appraising the straight forward cases of patent ductus arteriosus, coarctation of the aorta, tetralogy of Fallot or others that present the expected features of the particular condition. Many other congenital abnormalities or combinations of abnormalities remain that will have to be solved by special groups of cardiologists or laboratory investigators. Unusual cyanosis, clubbing of the fingers

or unexplained findings such as prominence of the pulmonary artery, general cardiac enlargement, marked electrocardiographic evidence of right ventricular hypertrophy or right bundle branch block should direct one's suspicion to congenital heart disease. For the immediate future and until simple clinical methods will prove adequate without catheterization or angiocardiographic studies, many puzzling cases in which the possibility of congenital heart disease comes up will have to be referred to special centers. This may well be true at times of cases of acquired heart disease as well. The physician must therefore be ready to seek additional guidance in the care of some of these unusual cases.

UNCOMMON CAUSES OF HEART DISEASE

When the more common types of heart disease have been satisfactorily eliminated, a variety of less frequent types of heart disease remains to be considered. Most of them for the present are incurable and therefore no great harm is done if they are overlooked. Among them are amyloid or sarcoid disease of the heart, scleroderma heart disease, carcinoid, idiopathic, virus or Fiedler's myocarditis, hereditary cardiomegaly and a host of other rare forms of heart disease.

Atrial Myxoma: There is one condition, though very rare, that now deserves greater concern, i.e., myxoma of the atrium, more frequently the left. Whenever there are transient episodes of faintness, cyanosis or breathlessness, especially if associated with a change of position of the body, the possibility of an atrial tumor must be considered. If the findings resemble those of mitral stenosis but come and go and there is no history of rheumatic fever and atrial fibrillation is absent, one should especially think of myxoma of the left atrium. If the clinical findings suggest primarily transient right-sided embarrassment with transient cyanosis, liver enlargement or increased venous pressure, a similar lesion may be present in the right atrium. Under these puzzling circumstances angiocardiographic studies would be justified for these lesions are completely curable by appropriate surgery.

Errors in Treatment

In the foregoing discussion errors in diagnosis were considered. It must be realized that often the correct treatment is given when an accurate diagnosis is not made. If there is no other therapy available for the particular condition apart from that generally employed for congestive heart failure, it does not matter whether amyloid disease of the heart muscle is overlooked. Similarly it is not important in the care of a cardiac with advanced congestive failure if an episode of "indigestion" that occurred several years before was not recognized as an attack of acute coronary thrombosis with myocardial infarction. The important errors in diagnosis that were emphasized previously were those that require a different treatment and for which effective treatment would be available if the correct diagnosis were made. There remain to be considered, however, errors in the treatment and management even when the diagnosis is correct.

CONGESTIVE FAILURE

Sodium and Potassium Intake: Most cases of ordinary congestive heart failure in general practice are now being treated properly. There are still many instances in which the patient fails to carry out the dietary advice to restrict sharply the intake of sodium. In some of these cases the entire fault lies with the patient. In others the physician has not emphasized sufficiently the importance of real salt restriction. Rigid attention to this matter may make the difference between recurring congestion and freedom from fluid retention. Loss of *potassium* from prolonged diuretic therapy with resultant asthenia and tendency to digitalis intoxication still takes place. The development of paroxysmal atrial tachycardia with block discussed previously often is a clear-cut indication of digitalis intoxication. It may be a life-threatening arrhythmia and is an indication for the administration of potassium or procaine amide and the discontinuation (at least temporarily) of digitalis. The opposite hazard must also be watched for, i.e., retention of potassium when there is marked oliguria. A marked elevation of the potassium level in the blood or peculiar tent-shaped T waves in the electrocardiograms can guide the physician in this regard.

Digitalis Administration: It is a common experience that patients in chronic congestive failure of a lesser or greater degree, who have been taking the so-called maintenance dose of digitalis daily, really are markedly underdigitalized. Frequently such a patient will not only tolerate but also be greatly improved by doses that are comparable to those one might

use in a previously undigitalized individual. It is surprising that in some cases of this sort, giving a 0.1 gm. dose of digitalis three times daily may be tolerated for several days or even a week and only then produce the hoped for improvement in compensation. In fact, it is good practice to try this method when a patient is not doing well, if you can observe the effect carefully and be in a position to detect any untoward effects from digitalis should they occur. It must be borne in mind that the requirements of digitalis differ very greatly in different individuals and also in different conditions. In each patient the administration of digitalis may well be regarded as an individual experiment in pharmacologic titration of the drug.

Thoracentesis: There are two well known procedures that are available in the treatment of congestive heart failure that are often neglected, i.e., thoracentesis and phlebotomy. It is very surprising that the same physician who, not many years before when he was a medical intern in training, had performed many phlebotomies and chest taps will hesitate or neglect to do those same procedures when he goes into practice. Furthermore, when this question does arise the home physician will think that the patient should be sent to a hospital to have it done or might even believe that a surgeon should be called. The practicing physician who may have done a hundred chest taps in his early years certainly should not need the help of a surgeon who has had less experience with the same procedure. Furthermore, this can be carried out quite readily in a patient's home if necessary even without the help of a nurse.

The existence of hydrothorax, especially on the right, is frequently overlooked. Even when present, the amount of pleural fluid is generally underestimated and its importance is too often belittled. Simple bedside examination is all that is necessary to detect hydrothorax. Definite dullness, decreased breath sounds and especially diminished tactile fremitus at the base of the right lung as compared to the findings at the left base in a chronic cardiac, almost always denote free pleural fluid. Only rarely will these signs be due to a high liver or some other disease in the lungs. When both bases present similar abnormalities, fluid generally is present in both pleural cavities. In most instances it is not necessary to take x-ray films of the chest. This is better done after the thoracentesis when the details of the lung, size of the heart and the question of calcification of the heart or valves can be more satisfactorily investigated. When in doubt, x-ray examination of the chest before inserting the needle would be indicated. If it is thought that more than 500 cc. of pleural fluid will be removed, tapping the chest is likely to help. There are instances in which not only will breathlessness improve immediately after the chest tap but other evidence of congestion such as pitting edema and engorged liver will then start lessening. It is not logical to deny the chronic cardiac relief obtained in this way by claiming that the hydrothorax will soon return. When it does, the procedure, while not difficult, can be repeated. One may be surprised that after some paracenteses, fluid may not return for months or even years.

Phlebotomy: This is another much neglected therapeutic procedure in the practice of cardiology. Some of the neglect may be part of the rebellion against the old custom of bloodletting that prevailed centuries ago and that was carried out for all sorts of illnesses, often with what must have been disastrous results. Some may be due to the fact that the exact criteria and therapeutic indications for phlebotomy are not clear and have never been thoroughly formulated. The present views therefore rest for the most part on clinical impressions. I have no doubt whatever but that removing 500 cc. of venous blood has been life saving in some desperately ill patients with heart failure that I have treated. I am also certain that phlebotomy has been very helpful in less critically ill cardiac patients with chronic congestive failure. Frequently it has been the starting point or the initial move following which improvement first began to appear.

The circumstances in which phlebotomy appears to be helpful are of two types. There are emergencies when there is *acute pulmonary edema* with marked dyspnea and suffocation and the blood pressure is elevated or at least has not fallen to hypotensive levels. If the condition has not responded to simpler methods such as tourniquets, aminophyllin, morphine, oxygen and having the patient put into a chair with the feet down, a brisk phlebotomy may be life saving. I have seen rare instances in which a moribund or unconscious person has promptly responded and become conscious in ten to fifteen minutes after a phlebotomy of 500 to 600 cc. The other group consists of individuals with more chronic *refractory heart*

failure, an enlarged liver and distended cervical veins. Here the favorable effect is not as dramatic or instant but nevertheless becomes apparent in hours or during the following day or so. In the latter group the venous pressure is decidedly elevated whereas in the former group it may or may not be so. In general, congestive heart failure is almost always accompanied by an increase in blood volume and with recovery of compensation the blood volume tends to return toward normal. One or two phlebotomies may be helpful in this readjustment. In cases of acute pulmonary edema venesection probably works by decreasing the return flow to the right side of the heart and therefore in the output to the lungs. In this way the imbalance between the output of the two ventricles is done away with.

It was stated above that the exact indications for phlebotomy have not been clearly defined. Obviously, one would hesitate to perform phlebotomy if there is significant anemia. It certainly would be contraindicated in the presence of shock or marked hypotension. If the arterial blood pressure is normal or preferably elevated and there is dyspnea or obvious evidence of pulmonary congestion, venesection should be safe and helpful. The same is true if the venous pressure is elevated and there is no shock. The difficult decision arises when both pulmonary congestion and shock are present at the same time, as occurs in some cases of acute coronary thrombosis. For the pulmonary congestion one would perform phlebotomy and for the shock one might want to administer a blood transfusion. Under these circumstances one would carry out the customary measures, such as the administration of oxygen, the use of intravenous pressor drugs and even ouabain or digitalis compounds. There have been rare occasions, when the situation remained precarious day after day and one was wondering whether to perform phlebotomy or give a blood transfusion, that the final decision to perform a phlebotomy proved decisive in initiating recovery. A final note may be interjected at this point. The blood obtained in bleeding cardiac patients generally can be useful for transfusion purposes and added to the blood bank. I cannot overemphasize the fact that venesection can often be valuable in the care of cardiac patients.

USE OF QUINIDINE

There are additional details in the treatment of patients with heart disease that deserve discussion. Insufficient or excessive dosage of digitalis must be watched for. This problem has already been considered. The use of quinidine in general practice leaves much to be desired. The attempt to regularize the rhythm when persistent atrial fibrillation or flutter is present generally requires hospitalization. Changes in cardiac rhythm that demand prompt recognition may occur suddenly and the exact type of arrhythmia may require electrocardiographic tracings to be taken at odd times. This is difficult if not impossible in patients' homes. It is best accomplished not only in a hospital but in one where a resident physician may be able to make these frequent decisions at odd times of the day. I will not take up the various schedules of quinidine dosage that are currently used. However, there are a few points that need emphasis. If the arrhythmia does not respond to a certain dosage in a day or two, nothing is gained and often ill effects result from continuing that same dosage day after day. The dose of quinidine should be increased or the drug should be discontinued entirely.

Maintenance Therapy: A more common error occurs when reversion to normal sinus rhythm has been attained and the patient is advised to continue a prophylactic maintenance dose of 0.2 or 0.3 gm. three or four times daily more or less indefinitely. Such patients (especially those with mitral stenosis) often revert to the former atrial fibrillation and continue to take the same daily doses of quinidine for weeks or months while the arrhythmia persists. When this occurs, the cardiac status is apt to deteriorate especially if digitalis is not being taken as well. The ventricular rate is likely to be faster under quinidine therapy while atrial fibrillation is going on than it would be without any quinidine. The physician who is treating such a patient may be entirely unaware that the rhythm has reverted to an irregular one and the patient continues to take the medicine outlined for him because he knows how much it helped him at the start. In fact, the physician himself may hesitate or fail to discontinue the use of the drug, recalling the very favorable result obtained originally. The general principle to be borne in mind is that moderate or large doses of quinidine do some harm while trying to accomplish some good. Quinidine, like digitalis, should be regarded as a cardiac toxin. It may be desirable to use even large doses of quinidine for a short period, actually making the patient

ill temporarily, to obtain a certain worth while result. If the desired result is not obtained after an adequate and justifiable course of treatment, the drug should be stopped entirely. A patient with atrial fibrillation who receives increasing or large doses of quinidine for two or three days may be quite ill during that time. But when a normal rhythm has been established and a small maintenance dose can maintain the normal rhythm, the patient may feel extremely well and have no more ill effects from the quinidine. The proper use of quinidine requires more intelligent guidance on the part of the physician and more cooperation by the patient than is necessary in administering digitalis.

Anticoagulants before and during Quinidine Therapy: A further point that now confronts the physician when trying quinidine for persistent atrial fibrillation is whether to use anticoagulants. There is no known statistical study that answers this question satisfactorily. There are rare occasions in which after reversion to normal sinus rhythm peripheral arterial emboli have occurred. This complication is particularly serious if the embolus goes to the brain. Although these are rare, I have no doubt whatever that the quinidine is responsible for this uncommon complication. In my own experience nothing serious has happened during quinidine therapy in nonvalvular cases. A few instances of hemiplegia, peripheral emboli or sudden death have occurred in cases of mitral stenosis. The purpose of giving anticoagulants would be to prevent embolization. It is not certain whether this can be accomplished. It is impossible to know whether there is a mural thrombus in the left side of the heart, unless previous embolization has already taken place. Furthermore, it is not known how long before quinidine is to be given the anticoagulant should be started. If it requires a lengthy preparation and can be properly undertaken only under hospital supervision, this involved treatment would not be considered practical in many instances. It has been my custom, though I am not sure it is the best course to follow, to give heparin in doses of 50 to 75 mg. intramuscularly every six hours beginning a day or so before quinidine is started until the quinidine is discontinued or until twenty-four hours after return to a normal sinus rhythm. I must confess that in some nonvalvular cases of atrial fibrillation I give no anticoagulants during the trial on quinidine therapy.

PULMONARY EMBOLISM

A very common and dangerous error in the care of cardiac patients is overlooking pulmonary embolism. This can occur as a single event or in a repetitive form. It can exist in the absence of any heart disease and present the picture of acute cor pulmonale. It then can resemble acute coronary thrombosis. When small emboli keep recurring, right-sided failure may develop as a result of chronic cor pulmonale. The problem becomes further confused because these pulmonary complications are frequent in patients with other and independent forms of chronic heart disease, such as valvular, hypertensive or coronary artery disease. It follows, therefore, that the possible presence of pulmonary emboli must be thought of in all chronic cardiac patients.

Clinical Diagnosis: The diagnosis of pulmonary emboli with or without infarction is often difficult and will not be taken up in all details in this discussion. The typical acute episode presents very few problems. The following clinical features are the common and more helpful evidences of an acute pulmonary embolism, i.e., sudden collapse, faintness or dyspnea with or without unilateral chest pain, subsequent cough and bloody sputum, a rising heart rate and slight fever for the preceding few days, signs of thrombophlebitis of the calves, electrocardiographic changes of acute cor pulmonale, x-ray evidence of pulmonary infarction or of localized ischemia of the lungs and an undue increase in the pulse and respiratory rate for the slight fever that is present. The difficulty becomes great when few or none of the clinical features are present or sufficiently distinctive. I have not infrequently overlooked pulmonary embolism despite careful observation. When daily observation of the legs fails to elicit evidence of thrombophlebitis and the x-ray film merely shows some congestion or quivocal changes compatible with infarction, atelectasis or pneumonia, it may be almost impossible to make a definite diagnosis. After some unhappy experiences I have come to the point that if a patient with congestive failure is not progressing satisfactorily, especially if auricular fibrillation, transient or persistent, is present, one would be justified in instituting a course of anticoagulant treatment. The thrombophlebitis may be occult or pulmonary thrombosis may be developing *in situ* from local changes and stasis. If carried out under careful supervision, there should be very little risk

and although the diagnosis might never be confirmed some patients with these otherwise fatal pulmonary complications might be helped.

Therapy: When there is satisfactory or suspicious evidence of thrombophlebitis of the legs, ligation of the femoral veins may prove to be the procedure of choice. Obviously if the emboli arises from pelvic veins or from the right side of the heart or if the pulmonary arterial occlusions are due to local vascular thrombosis, ligation of the veins of the legs or the inferior vena cava will be of no avail. Under these circumstances the only recourse available is prolonged anticoagulant therapy.

Differentiation from Coronary Thrombosis: There is one small group in which the error in distinguishing an acute pulmonary from an acute coronary episode should not be frequent. Individuals who suffer some serious cardiocirculatory-pulmonary complication a few days after a traumatic injury, such as a fractured leg, should be suspected as having a pulmonary embolism. Too often the diagnosis of acute coronary thrombosis is made because of sudden chest distress, slight fever and leukocytosis and electrocardiographic changes. The latter changes may be those seen with acute cor pulmonale and do resemble those seen with acute posterior myocardial infarction. The intimate relationship to an accident, especially if a limb has been immobilized in a cast, should direct the physician's attention to the possibility of local thrombophlebitis and pulmonary embolism rather than a coronary attack. This differentiation has not only vital therapeutic implications but presents important medicolegal considerations when the question of death from accident arises.

In the discussion of acute pulmonary embolism, mention should be made of a peculiar but uncommon type of respiration that may be observed. I have seen a few instances in which the breathing was gasping and resembled the behavior of a fish struggling for air out of water. There is a sudden gasp with the mouth open but on auscultation very little in the way of breath sounds is heard. I do not recall seeing such breathing in other conditions.

Errors in Prognosis

Errors in prognosis are common and bring the medical profession into ill repute in the eyes of the lay public. Mistakes in diagnosis or treatment often go unrecognized either by the physician or the patient and his family. A postmortem examination is rarely done in general practice and the overlooked coarctation of the aorta or any other curable condition is never discovered. Even when the basic diagnosis is not in error and the patient had no more than hypertensive heart failure, the fact that a hydrothorax of 2,500 cc. was present, the removal of which might have given comfort and prolonged life, may never be known to physician or family. However, when a physician gives a grave prognosis or worse still indicates that a patient is going to die and the patient recovers, the entire medical profession often suffers greatly. The family, realizing that there is nothing to be lost, may resort to Christian Science or to chiropractic or, having discharged the physician, may start administering some odd kind of syrup suggested by a neighbor or an old aunt. If this change in medical care happens to come at the right time when the illness, though critical and serious, proves to be one from which spontaneous recovery may take place, it is not surprising that from then on that family will worship at the shrine of "irregular medical practitioners" and have no faith in the regular medical profession. The Christian Science healer cured the patient when the doctor had given him up. This can happen in a large number of self-limited diseases.

I recall an instant in which a mother became a Christian Scientist because her child who was desperately ill with acute rheumatic pancarditis and a large pericardial effusion was given up. At one point the condition was very critical and the physician told the family that the child was going to die. Through the influence of some relative of the family the physician was discharged and a Christian Science healer was called in. Just about that time the condition started to improve. The child made a complete recovery and the mother thereafter would have nothing to do with the medical profession.

The inference from the above is that physicians should hesitate to try to take on the role of the Lord. We are physicians and not prophets. There is much that we do not know and it is wise for us to indicate our limitations in our conversations with our patients and their families. It is well for us to be hopeful though at times we must be cautious. It is generally best to keep the door a little ajar even under the darkest circumstances. We have all seen the patient with the severest kind of acute coronary thrombosis recover and contrariwise the one with the apparently mildest suddenly die.

Patients often ask us how long they can live after a coronary attack. We should answer that we do not know but that many live a great many years in good health. It is always better and less harm is done if we are on the side of being too optimistic than too pessimistic. Provided no error in treatment is made, the patient will have happier and more useful years if he lives in the spirit of hope than of despair.

Franz Groedel Memorial Lecture

The Humanities in Medicine*

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IN THE spring of 1260, the University of Padua, as it had done for some forty years, opened its doors to aspiring students of medicine who had completed the secondary school. The curriculum or course of study included the *Trivium*, consisting of grammar, rhetoric and dialectics and the *Quadrivium*, or arithmetic, geometry, astronomy and music. Together these subjects made up the seven liberal arts. The language was Latin. Medicine was taught as a branch of philosophy and consisted almost entirely of lectures and readings of such authors as Galen, Hippocrates, Avicenna and Rhazes who had lived and written centuries before, with cursory reading of some books on medical practice usually by more modern writers. Anatomy was taught by demonstration. The only textbook on the subject was not to be published until over one hundred years later, although presumably the material was available in manuscript form, having been completed in 1316. Courses and textbooks were usually determined by Papal Bulls. Graduation required a defense of four theses of Aristotle, Hippocrates, Galen and a modern writer. The successful candidate was awarded a doctorate in philosophy and medicine and was recognized as a member of a learned profession and an educated man.

In 1960 the approved medical curriculum in the United States contains (except as to be noted) only biologic and physical sciences and the application of those sciences to the prevention, diagnosis and treatment of disease. In relation to psychiatry, and otherwise to a limited extent in some schools, psychology, sociology and anthropology are included; courses in the history of medicine are sometimes offered. The degree of M.D. is conferred on successful completion of the course and a period of supervised practice and some additional study of much the same subjects are customary before beginning the practice of medicine. The new doctor of medicine is recognized as something of a scientist and a good technician but there may be some doubt whether he is an educated man.

Definitions of Terms

There does not appear to be any good, concise, simple definition of humanities. Everyone has an idea what it means, but to put it into words is somewhat difficult. There are, in fact, two definitions. One is technical and refers to a number of disciplines or studies which are usually included under the term *the humanities*. They are the Greek and Latin classics, grammar and rhetoric, literature, history, ethics, politics, art and music. These are to be distinguished from science and theological speculation. There is, however, some uncertainty as to exactly what studies should be included and the list seems to have changed with the times or the inclinations of the writer. The second definition refers to an attribute applicable to man, for which perhaps the best single word is "humaneness."

These two definitions can each be related to a separate and particular aspect of medicine. The technical definition, a group of disciplines or studies which make up the humanities, can be related to the study of medicine or medical education. The second definition, "humaneness," is applicable to the practice of medicine. I propose to examine these two aspects of the humanities in regard to the two fields of medicine to correlate the two definitions in the relation, to some degree, of cause and effect.

Leaving the question of what particular sub-

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jects are included in the term humanities, it is apparent that the medieval course in medicine included much that was cultural and not directly related to medicine as we know it. Yet, it must be remembered that that was *the* medicine of the day. If astronomy or dialectics or music was taught and required, it was a part of medicine and knowledge of these subjects a part of the proper knowledge of a physician. They were not added as something interesting or as desirable electives. If Latin was the language, it was not used for its cultural value; it was the common language of the learned and educated. The study of medicine was a true education, and medical practice a profession in the true sense of the word, not a trade or a handicraft.

I will clarify my use of the term medical education and the word physician. In any comparative analysis of medical education over the years or in different areas of the world, it is necessary to make certain allowances, to discriminate between different levels of medical education, different kinds of practice of the healing arts, to arrive at some common denominator and allow for changing definitions. It would be manifestly unfair to compare the education, or better training, of a barber surgeon of the seventeenth century with that of a 1960 graduate of Harvard Medical School. It would also be unfair to compare the education of today's naturopath with that of a sixteenth century physician such as Vesalius. It should be noted that even today there are, worldwide, relatively as great differences in the education of practitioners of the healing arts as there were during the Renaissance or the eighteenth century. For my purposes, any contrasts I may draw between medical education at various times will be between the best medical education of the periods under discussion.

Some people would remind me that the modern student of medicine must acquire a general education before entering medical school, including certain higher studies, some of which can be classed with the humanities. It is from these studies, together with the others of the college curriculum, that the student is expected to become an educated man and later an educated physician. First, let me point out that the medieval student of medicine also had a certain premedical education, the *studium generale* and the *studium particulare*. In these, presumably, he acquired a sufficient facility in the required basic tool subjects to allow him to pursue the study of medicine but they were not those of higher education. The humanities were a part, indeed, the largest part of the course in medicine and were, in essence, the cause of his being an educated man in terms of the day.

History of Medical Education

Before returning to the matter of the modern premedical curriculum, let me follow very briefly and sketchily the development of medical education through the ages.[1] If in *medieval* medical education there was little study of science, it was because the body of scientific knowledge was small, and that which might have been discovered was kept unknown by tradition and ecclesiastic dogma. According to Garrison,[2] the great advances of the Renaissance and the Reformation came as the result of the work of the so-called medical humanists, actually the Greek scholars coming to the West after the fall of Constantinople, yet it is notable that the advance lay in the growth of *science* and the development of the spirit of *scientific inquiry* and objectivity. This is best represented by the anatomy of Vesalius and his school and by that of Da Vinci; by the surgery of Paré and the chemistry of Paracelsus. Dissections became more frequent, there were occasional necropsies and some bedside lecturing. The teaching of botany was introduced. Nevertheless, the medical humanists still were men of letters and many, such as Linacre, remain best known for their work as grammarians, philologists and translators of Latin and Greek.

The seventeenth century saw the decline of the universities in relation to the study of medicine largely because of their failure to keep pace with the development of science, marked as it was by such milestones as the brilliant deductive thinking and experimental work of Harvey, the invention of the microscope, the development of microscopists such as Van Leeuwenhoek and the growth of chemistry as represented by Boyle and Hook. With the decline in the university there occurred organization, growth and spread of the scientific society, some of which, with their transactions, exist to this day. Dissatisfied with the teachings of the universities, restricted to classical studies and sterile lectures on outmoded works of the ancients, physicians and men of education met to discuss new experimentation and, it should be noted, "the ornaments of elegant literature and philosophy which, like a graceful garment, adorned the whole body of science."[2] The physician of the seventeenth century distinguished himself as a

mathematician and astronomer, a physicist, a microscopist or a chemist, but he also might teach philosophy, philology and archeology as well as medicine.

The eighteenth century, if it failed to maintain the pace of advance in science exhibited by the seventeenth century, managed to progress in physics and chemistry particularly, while at the same time maintaining the position of the physician as an educated man. The physician was a man of letters, for example, Goldsmith, Schiller and Göethe. Other men of letters were practitioners. Von Haller was an anatomist, physiologist and botanist, but he was also a poet and writer of historic novels. It is worth noting that in 1743, Louis XV separated the surgeons from the barbers and wigmakers "who were forbidden to practice," and made a Master of Arts a requirement for a Master in Surgery. Thereafter, the surgeon was a "lettered man" prepared for his lifework by a special *scientific* education. In medical education the century made its greatest advance in anatomy and clinical medicine. Bedside teaching was introduced between 1745 and 1798. Private instruction, which was extensive, was essentially completely medical.

Development of American Medicine: The medicine and medical education of the *nineteenth and twentieth centuries* are so recent as to be familiar to all of us. There was no American medicine, in the sense of which I am speaking, in the colonial period. Such medicine as existed was the same as the European medicine from which it was derived except for the uneducated or self-trained practitioners with no pretense to medical schooling or a degree. They, of course, had their counterparts in Europe except that in America there was probably less charlatanry and quackery than in Europe and more honest effort to use native wit and intelligence under conditions enforced by a young, raw, frontier society which demanded some kind of medical practice. Not until the establishment of medical schools at the end of the eighteenth century did American medical education begin to take on a distinctive character of its own. Even then, it closely resembled, except for certain aspects of the premedical education, the English or French model until its decline with the rapid expansion of the population. This in conjunction with the push to the West, the occupation and settlement of new lands and the expanding frontier caused an irresistible demand for more "doctors" which led to the debasement of medical education in the United States. Three of the first five medical schools established in the United States were founded by universities or colleges (Kings College became the medical faculty of Columbia University) and probably possessed a greater degree of excellence in relation to the times than was to be found in American medicine for many decades thereafter. The continuing pattern of medical education, and with it the educational level of the physician in the United States, is one of less and less *education* and more *training*, with few exceptions. There was, until the latter half of the nineteenth century, a concomitant betterment in technology, but even this disappeared to a large extent in the rash of "diploma mills" of the late 1800's and early 1900's. Only with the advent of the Flexner report and the development of university type of medical school, initiated by the Johns Hopkins, was there a decisive improvement. The primary effect was on the teaching of medicine *per se*, and soon in the twentieth century began the phenomenal advance of science which still in this decade shows no signs of abating in medical education today. In fact, on another occasion when I had an opportunity to review the present medical education in this country,[3] I questioned whether the progress we had made toward a university type and an *educational* type of medical education following the medical renaissance and reformation of the 1920's and 1930's had been maintained. Whether, under the press of the vast increase in science, the increasing length of medical study and the burden of rising costs and inadequate funds, we may not have failed to reach the high level of medical *education* to which we had aspired.

I think it has been apparent, as I have briefly sketched the development of medical education from medieval times to the present, that an ever increasing growth, development and extension of science has been accompanied by a reciprocal decline and diminution in those elements of education which can be included in the term "the humanities."

Premedical Education

Under present conditions, premedical education provides the only opportunity for acquiring a general education of the kind desirable for the student of medicine. I mean, of course, the only organized course of study. Individual students may, by their own initiative and endeavor, acquire such education as they wish. In this country particularly, and at this time

with almost no exception, admission to medical school requires a minimum of three years of college. Some schools require the bachelor's degree or satisfaction of the requirements for the bachelor's degree at the completion of the first year of medicine. A few are satisfied with nothing less than the bachelor's degree.

What does this actually mean? The only required premedical subjects for admission to approved medical schools in the United States (there are no unapproved schools) are a single theoretic and laboratory course in inorganic chemistry, organic chemistry, physics and biology. No classical languages and no modern foreign languages are required; neither history, philosophy, art nor music are requisites. For other than the sciences, dependence is placed on the requirements of the college either for a degree or for continued enrollment in the college. It is true that additional courses are required by some medical schools and often are recommended if not required. They usually are additional courses in the sciences and mathematics. Even when such approving agencies as the Association of American Medical Colleges and the American Medical Association recommend that more time be given to the humanities and cultural subjects, the student is disinclined to follow that advice for fear that the voice is Jacob's but the hand is Esau's.

Two aspects of the premedical curriculum which affect its adequacy and suitability as a means of securing a satisfactory level of general education for medical students and physicians, *other* than the number and kinds of subjects, are the quality of the courses and the quality and character of the teaching. Unfortunately, in many instances the quality of the individual courses is not such as to engage the interest and stimulate the student to serious study and a mastery of the discipline in considerable depth. Usually, only the introductory course is available (partly because of time) and sometimes a special course, designed for those who are preparing for professional studies, is provided with a level of excellence below that offered to the general student. All too often the premedical student chooses those courses. Actually, the students often are directed or influenced to enroll for such typical premedical courses by their advisors. Altogether the result is apt to be inadequate to produce an educated physician.

Sir Richard Livingstone[4] has pointed out that the *way* a subject is taught is perhaps equally as important as what is taught, and questions whether in the area of premedical education it is taught in a way to secure the desired results. It may be as he says, that there is no use teaching anything if you teach it badly and the converse, that it does not matter what you teach if you teach it well. According to Livingstone, the aim of teaching nonscientific subjects to those primarily interested in science should be less the acquisition of a collection of facts than to arouse their interest and awaken their minds so that they will be led to pursue the subject further on their own volition and continue this interest on through life.

Objectives of Medical Education

Abraham Flexner said that medical education was not so much a matter of medicine as of education, and therein lies the essence of our problem and a succinct statement of the situation. The pressing question before us is whether we want and need a trained doctor or an educated doctor, a technician or a member of a learned profession. What are the differences? What are the advantages and disadvantages of each? Is the true objective of medical education to produce an educated man with an excellent technical knowledge of the sciences and their application to the practice of medicine, or, in this day of highly developed science, is the training of a competent technician to have preference to the extent of neglecting real education? The difference, it seems to me, lies in the relation of man to man, of man to the world and to the society in which he lives, and of man to himself.

This brings us back to the second definition of humanities. In the plural form, it can be defined as "human characteristics and attitudes," but its truly significant meaning is in the singular form which means the quality of being human, the peculiar nature of man by which he is distinguished from other beings, and the kind feelings, dispositions and sympathies of man.

Sir Richard Livingstone has pointed out that man is composed of three elements: his body, his mind and his soul which, combined with our personalities, make us what we are. These three needs determine the aims of education, which should prepare us to make a living, to acquire some understanding of nature and the world around us, and help us to become good human beings. Such an education will train the powers of observation, of reason and of

imagination, and improve the ability of expression to meet the needs of effective behavior. But according to Sir Richard that is not enough. An education, says he, is not complete unless it gives people a philosophy of life. For the true physician, a philosophy of life must be one which enables him to love his fellow men, to understand their aspirations, their joys, their weaknesses, their strengths and their sorrows. He must learn to understand and appreciate their motives and the doubts and fears which sway them. He must know man not only as a compound of chemicals, or as a biologic unit but as a sentient being, a political animal, an essentially religious animal, whatever his belief or creed. Herein lies the art of medicine in its truest and best sense. Herein are the ethics, not the etiquette, of medical practice.

It is to this end that education becomes essential; education, not technical training—an educated physician, not a trained technologist. I do not mean that education is requisite to being humane, to having the quality of humaneness. There can be an inborn humaneness, kind feelings, a disposition of empathy and sympathy and understanding of man. One of the most humane men I know, a friend of long standing, learned to read and write only within the time of our acquaintance; but the proper practice of medicine requires more than that. It needs a broader and deeper understanding, a greater insight, a larger perspective, which can be obtained with a liberal education. (I should add that such an education does not guarantee humaneness. There can be well educated scoundrels and fiends.) There is good evidence that present day education is not accomplishing this result. Horvarth[5] asked if our medical students, when they leave school, know enough about the human to balance their extensive knowledge of the subhuman. As Petrarch said, "what, pray, will it profit to have known the nature of beasts, birds, fishes and snakes but to be ignorant or despise the nature of man—why we are born, whence we come and whither we go?"

Perhaps decay is inevitable. It is true that many times in the past medical education has been viewed with concern and dire predictions made of its decline; predictions which *apparently* have not been borne out. We are all familiar with accounts from the past, recording problems and situations which seem to have been the same as those of today, the implication being that today's warnings are merely the cry of wolf. However, it is characteristic of human nature to accept things as they are, not easily being able to appreciate how they might have been, had not certain things changed. Is it not possible that our eyes have been blinded to the loss of better education by the dazzling light of scientific and technical advance?

Science and the Physician

Perhaps as science grows, education of the kind that is essential to the making of a true physician must decline. Certainly, as science grows and is applied to medicine, the doctor becomes more remote from the patient, more and more impersonal. Man is not a machine or an animal, but the phenomenal advances in science tend ever to place him in that status in relation to the practice of medicine. In this respect the prospect is indeed alarming. It is perhaps appropriate that I address cardiologists, practitioners of a specialty which is an example of early and extensive instrumentation, tending to remove the physician from personal contact with the patient. I am sure, however, that everyone will agree with me that there is more to the practice of cardiology than electrocardiograms and cardiac catheterization, that much of it is the human, person-to-person relationship with the patient.

Even more instrumentation is in prospect. Perhaps some of you have read of the hospital of the future in which doctors and nurses will not make rounds, in which the patient will be "looked in on" by closed-circuit color television; pulse, respiration, temperatures, the electroencephalogram and electrocardiogram, etc., will be recorded by means of transducers, taped and analyzed by a computer and reviewed by a distant monitor.

I am not opposed to the advance of science and the greater application of science to medicine, to the care of the sick and the relief of pain and suffering. The more science the better, and, in fact, a liberal education facilitates and improves the study of science and makes a better scientist. But, as science grows, true education must accompany it. Only with education can we control the powerful tool of science which, improperly used, may cause disaster. Science must augment not displace education.

As a formula, science plus a liberal education, or better, a liberal education plus science makes an educated physician. This does not mean the addition of the social sciences to the medical curriculum. Valuable as they are and as

strongly as I believe in their need and importance, they cannot take the place of the humanities in securing an education of the kind I mean, although they may contribute to it. They remain sciences, albeit social sciences, and can be, although they should not be, as cold and impersonal in their application as electronics. They, too, in their practice must be guided and tempered by the humaneness obtained from a liberal education.

It is then the responsibility of our educational program to preserve and foster true education and the development of an educated physician.

Outlook for the Future

Recently I had the opportunity of commenting on my father's education in comparison with mine. Fortunately, there was no high school available to him, so he was sent to an academy some distance from his home. His was a "classic" course with Latin and Greek, drilling in grammar and English literature and French, adequate or better mathematics and solid history. At the university he had a course in "Ethics, or the Science of Beauty." He could quote Chaucer and had a good understanding of history and the historical perspective. He could even remember the names of the three continental soldiers who captured Benedict Arnold; not, of course, anything of any significance in itself except that it may indicate that the course was well taught and gained his interest. His science was good according to the knowledge of the day. His course in medicine could not compare with mine, in terms of the volume of knowledge, facts and theories; but it was among the best of the day. The difference between us is that he was, at least, a considerably better educated physician than I. It is easy to define the ideal student as Whitby[6] has done: cultured, broadly educated in the humanities, intelligent and intellectual, of transparent integrity, humane and sympathetic and, above all, one who will love his profession as well as his fellow men with all their weaknesses, joys and sorrows. The same could equally apply to the ideal physician. Not all could attain such an ideal, but it is the goal toward which we should strive. Unless we succeed in producing students and physicians with at least some measure of these qualities, we shall not succeed in producing educated doctors.

In my opinion, this remains the most pressing problem in medical education and medical practice today. Just how this is to be done, I do not know. I do not believe that the deficiencies in general education of medical students and physicians can be corrected by shortening the course in medicine, or by rearrangements of the subjects within the seven or eight years of premedical and medical studies. On the contrary, it is my belief that the course in medicine should be lengthened to the extent of at least utilizing the summer vacation period for an organized, systematic program of study. There does remain, however, in the area of general education, the opportunity of altering the program of primary, secondary and college education to effect a considerably greater degree of education at the end of the college period without the sacrifice of time, indeed with some savings.

Personally, I am not very hopeful of the future. The decline in morals and manners, the weakening and lowering of personal and public standards, of conduct and behavior, the acceptance of the second rate, the greater concern with getting something rather than how it is gotten, of material rather than intellectual and spiritual values, are symptomatic of an aging civilization. Civilizations would seem to resemble the people who compose them. They are born, they grow, they grow older. As they grow older, they display the signs and symptoms of social disease which ultimately cause their demise. Rarely is the course of the disease reversed and then only for relatively short periods. I am fully aware of amusing quotes from decades or centuries back which describe conditions seemingly much the same as those of the present, but without the dire results predicted. It is pertinent to ask where those civilizations are now.

In my opinion the signs are discouraging. However, I do know that unless steps to reverse this trend are taken at once, unless those who by their eminence, by their authority, by their ability and their power to change things act with promptness, decisiveness and wisdom, medicine as it should be will be gone forever and only technology will remain. "What shall it profit a man if he shall gain the whole world and lose his own soul?" What shall it profit us all if we gain the whole world of science and lose our collective souls?

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1. This description and the preceding are not intended to be taken as historically correct in every detail. It is a free rendering of material taken from Garrison, F. H.[2]

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Progress Notes in Cardiology

Edited by EMANUEL GOLDBERGER, M.D., F.A.C.C.

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Sudden Death in Infants and Children Due to Endomyocardial Fibroelastosis

DR. LOUIS GOODMAN (South Side Hospital, Pittsburgh) has recently described endomyocardial fibroelastosis as a constant, significant finding in sixteen of nineteen patients, ranging in age from stillborn to eighteen years, who died suddenly or with unexpected rapidity. Twelve were dead on arrival at the hospital.

Two of the three patients who did not have endomyocardial fibroelastosis had died of asphyxia due to food aspiration. The third died of acute ulcerative tracheobronchitis and pneumonia after a relatively prolonged illness. In contrast, the presence of endomyocardial fibroelastosis was associated with swift death in two other patients with similar respiratory infections, and in an infant with prodromal lesions of measles.

In five so-called crib deaths ascribed to mechanical suffocation, the infants were found to have endomyocardial fibroelastosis and mild interstitial pneumonitis. It is believed that in these cases the mild and usually subclinical respiratory infections triggered an underlying disorder in the myocardium which had been responsible originally for the endomyocardial fibroelastosis.

The finding of endomyocardial fibroelastosis as the exclusive pathologic change in a premature stillbirth and in two infants twenty and twenty-one hours old, respectively, suggested the possibility that this disorder might be a more frequent cause of intrauterine and perinatal death than has been recorded.

Sudden death in one four month old infant was associated with glycogen storage disease of the heart accompanied by very severe endomyocardial fibroelastosis. This suggested the possibility that the cause of death in these patients might not be the endomyocardial thickening, but an underlying disorder of the myocardium which could be metabolic or circulatory in nature, causing myocardial necrobiosis and secondary endomyocardial thickening.

The other cases reported indicated possible relationships between endomyocardial fibroelastosis (or preferably, the causes of endomyocardial fibroelastosis) and cardiac arrest during surgical anesthesia, minor surgery, exertion, or even simple diagnostic procedures such as spinal tap.

In one case, the presence of prodromal lesions of measles in a four and a half month old infant indicated that even a viral disease in the earliest stages may trigger the mechanism for unexpected rapid death in a patient whose deficient myocardial reserve is evidenced by the presence of endomyocardial fibroelastosis.

A curious periodicity was noted in the ages of the patients, suggesting the possibility that the life expectancy of a person with endomyocardial fibroelastosis, who survives the stress of birth, increases substantially with each day of life, at least for the first few years. The most critical period, however, is during the first six months.

It is believed that endomyocardial fibroelastosis may frequently be overlooked as a result of rapid postmortem hemolysis and myoglobinolysis. Restoration of the original color of the thickened endocardium may be quickly accomplished by placing the specimen in 10 per cent formalin or Jores solution for twenty-four hours or less. Obviously, final confirmation of the diagnosis must be made by elastic tissue preparation.

Although endomyocardial fibroelastosis was found in 84 per cent of cases of sudden or unexpected rapid, natural deaths occurring in infants and children ranging in age from still-

born to eighteen years, it is regarded as a phenomenon secondary to underlying myocardial damage and is not considered to have been the cause of death *per se* in any of these patients.

It is believed that the basic damage to the myocardium may be caused by a variety of factors, either congenital or acquired, including demonstrable and nondemonstrable anomalies of coronary artery distribution, congenital cardiac deformities altering ventricular blood flow, systemic or myocardial hypoxia, and metabolic disturbances of cardiac muscle.

Whatever the underlying defect may be, the mechanism for sudden or rapid heart failure in these patients may be triggered under certain circumstances by mild or severe respiratory infections, viral infections, anesthesia, minor operative procedures, spinal tap, exertion and possibly even shock or fright reactions. In most cases, endomyocardial fibroelastosis may be the only visible evidence that the functional reserve in the weakened myocardium was low.

The diagnosis of accidental mechanical suffocation in crib deaths should not be made unless the evidence is conclusive and endomyocardial fibroelastosis has been excluded as a possibility by autopsy examination. The unfortunate practice of attributing such deaths to accidental mechanical suffocation can only add unwarranted guilt to catastrophic tragedy.

Thyroid-Digitalis Antagonism: Its Modification by Reserpine

Drs. Robert L. Frye and Eugene Braunwald (National Heart Institute) have recently described the relationship between digitalis and thyroid activity on a specific cardiac property, the refractory period of the atrioventricular node. This was assessed quantitatively. The basal ventricular rate in patients with atrial fibrillation provided an index of the refractory period. Five euthyroid and one myxedematous patient with atrial fibrillation were digitalized with digoxin and their basal ventricular rate determined during a control period. After 100 to 250 μg. of tri-iodothyronine was administered daily, the basal ventricular rate rose to an average of 137 per cent of the control value. In order to return the refractory period of the atrioventricular node to the control level in three patients, the daily dose of digoxin had to be increased to an average of four times the control dose. In two patients, parenteral reserpine abolished this increased digitalis requirement. Also, the increased requirement of digitalis induced by a single large intravenous injection of tri-iodothyronine was abolished or diminished by parenteral administration of syrosingopine for approximately one week prior to giving tri-iodothyronine. In one undigitalized, myxedematous patient with atrial fibrillation, 0.58 mg. of acetylstrophanthidin was required to slow the ventricular rate to 70/min.; 1.50 mg. was required after the patient had been rendered euthyroid with tri-iodothyronine.

They conclude that digitalis and tri-iodothyronine exhibit antagonistic actions on the refractory period of the atrioventricular node. Since depletion of peripheral norepinephrine by reserpine abolishes this antagonism, it appears that these thyroid effects may be mediated by norepinephrine. It is suggested that very large doses of digitalis or a combination of reserpine and digitalis will be therapeutically effective in the thyrocardiac patient.

Book Reviews

L'Électrocardiogramme Dysmétabolique. Perturbations Ioniques et Électrocardiogramme, by A. Larcan and C. Huriet. Masson & Cie, Paris, 1959, pp. 222, 2500 fr.

This is an authoritative review of the possible correlations between electrolyte disturbances and electrocardiography. After outlining the physiologic principles involved, the authors compare them with the actual clinical findings, drawing on forty-four case histories from their own practices.

The first and longer part of the book is dedicated to potassium. The second part discusses the other electrolytes, i.e., calcium, magnesium and others.

The authors point out that an electrocardiogram indicative of blood potassium imbalance cannot be regarded as evidence of the fluctuations in the potassium level of the blood, but would rather appear to be a fairly faithful reflection of variations in the intracellular K: extracellular K, the "potassium gradient." This view is derived from comparisons between the data obtained by the method of determining the balance of intake and elimination and the results of neuromuscular excitability measurements during the course of various pathologic conditions such as renal insufficiency, digestive dyskalemia, periodic paralysis, hypo- and hyperglycemia and particularly diabetic acidosis. Since the electrocardiogram is an accurate and sensitive means of studying the depolarization and repolarization of myocardial cells, the authors do not regard the "dysmetabolic electrocardiogram" as a reflection of this or that humoral imbalance, but as evidence of a disturbed cellular metabolism. This significant clarification will therefore be of interest to all those concerned with the physiology and physiopathology of electrolytes. A bibliography of 511 references is included.

R. Heim de Balsac, M.D.

Acute Pericarditis, by David H. Spodick. Grune and Stratton, Inc., New York, 1959, pp. 182, $6.50.

The author apparently wished to publish a handbook on pericarditis covering the subject well without attempting to cover the subject in every detail. In this light, the monograph may be considered a small reference book. Chapters include anatomy and physiology of the pericardium, pathology of acute pericarditis, the electrocardiogram in pericarditis, pain mechanisms, characteristics of the friction rub, clinically dry pericarditis, pericarditis with effusion, roentgen manifestations, special diagnostic and therapeutic procedures, various types of pericarditis and classification of the pericarditidies.

The material seems to be carefully presented in easily understood language. The illustrations are of good quality and are clear. Although roentgenograms are used somewhat freely for a book of this size, more could have been used to advantage. A good list of references is presented.

The book compares well with small monographs covering limited subjects. It will be especially useful for the student and general practitioner, but is of value also for the internist and cardiologist. Elwyn Evans, M.D.

Electrical Impedance Plethysmography: The Electrical Resistive Measure of the Blood Pulse Volume, Peripheral and Central Blood Flow, by Jan Nyboer. Charles C Thomas, Springfield, Ill., 1959, pp. 243, $7.50.

Dr. Nyboer has maintained an unflagging interest in electrical plethysmography for twenty years despite the indifference of the medical community. He has performed much of the original research both in instrumentation and biophysics, has written many articles and has based many scientific exhibits on his experience with this method. The book details all of these plus many other studies on the clinical applications of the plethysmographic method in the study of the human circulation in health and disease.

Since Dr. Nyboer has extensive personal experience in this field, the book is authoritative. No one is better qualified to present a monograph on this subject.

This is not an easy book to read, nor probably was it so intended. Much emphasis and space are devoted to the mathematics of impedance,

inductance and capacitive characteristics of the various body tissues. Additional sections carefully delineate the electronics of the various instrumentations that have been applied to the study of this problem, with particular emphasis on the high frequency system developed by the author and Mr. Bagno. Experimental evidence, both physical and biologic, of the validity of the electrical method is presented in detail.

The monograph is an essential text for any worker who intends to explore this field. In addition, those physicians who keep abreast of the latest advances in cardiovascular physiology will want to own this book. It does, however, contain numerous typographical errors which should be corrected in subsequent editions.

SIDNEY ARBEIT, M.D.

Electrophysiology of the Heart, by Brian J. Hoffman and Paul F. Cranefield. Blakeston Division, McGraw-Hill, New York, 1960, pp. 323, $12.50.

It should be noted that this book is not being reviewed by an electrophysiologist, but by a cardiologist who has been studying various aspects of electrocardiography for twenty years. This background perhaps explains the great academic and practical value which the reviewer believes exists in this excellent publication.

The nine chapters must be read and studied slowly as the material is abundant and the problems to be resolved are complex. The major substance is the study of the transmembrane action potential of the different tissues such as auricular, ventricular, S-A node, A-V node and Purkinje fibers. The different morphologies of phases 0, 1, 2, 3 and 4 are demonstrated as having major importance and, moreover, must be in agreement for a correct electrocardiographic interpretation.

The first chapter is devoted to the methodology involved in registering the special phases by means of microelectrodes. There is a discussion of the action potentials obtained across the cellular membrane in the different cardiac fibers. There is also a section which discusses the unipolar electrocardiogram and once more returns to the observation which the majority of physiologists make, namely, that the remote electrode is influenced by changes in potential which originate in the tissue itself. The viewpoint of the electrocardiographer is different since it is well known that the potential of a given field falls rapidly and in relation to the square of the distance between the electrode and the site from which the potentials originate. Thus, the influence of the cardiac potentials on the distant electrode is always negligible and when the proximal electrode is directly on the heart one may put the distant electrode on any part of any limb of the experimental animal and the curve recorded will always be the same.

In the same section the authors discuss the relationship between the transmembrane potential and the electrogram and the reason the latter may be considered as a derivative of the monophasic potential. When the derivation is unipolar it is necessary to consider the laws that govern the volume of the conducting media and, therefore, such relationships can only be discussed as analogies. It should be noted that this type of derivation when analyzed by Poisson's Integral has been shown to have great usefulness in electrocardiographic interpretation.

Chapter 2 is devoted to a discussion of excitation and conduction. The electric properties of the excitable cells are studied as well as the core conductor properties; it is emphasized that the transverse resistance of the membrane is higher than the longitudinal resistance on both sides of the membrane. This means that the flow of current will spread along a relatively greater length of fiber (electronic spread). The electric models of the membrane which correspond to a resting and excitable cell are so clear and simple that they could easily be used as teaching material for any level of student. The importance which is given to the ionic gradients and the electromotive force resulting from the gradients of permeability of Na and K is quite correct as an explanation of the principal events.

Chapters 3, 4, 5, 6 and 7 study the action potential of the atrium, ventricle, S-A node, A-V node and the Purkinje fibers, respectively. All of these chapters are similarly constructed: after the description of the characteristics of the curve, the authors detail the changes due to frequency, temperature, drugs, ionic changes, effects of current flow, acetylcholine, epinephrine, etc. For each of the potentials there is given a great variety of useful data from which I shall choose only a few appropriate and important examples.

The authors show that the triangular form

of the atrial action potential (recovery phases 2 and 3) cannot be identified. This may be related to the lack of the auricular T in the peripheral electrocardiogram.

The conduction velocity in the ventricle of the dog is somewhat higher than the classically accepted values and close to 0.9 to 1.0 M./sec.

The authors insist on the necessity of distinguishing between conduction velocity and measurements of excitation time (sequence of activation). They believe that plunge electrodes produce local injury and block. We have used this type of electrode and it does not appear to cause a significant degree of injury since the unipolar derivations obtained from it do not exhibit changes in the RS-T segment. On the other hand, our results are also in agreement with other workers in that the degree of block is also not very significant.

In the sinoatrial node the pacemaker fails to maintain a steady level of resting potential (slow depolarization). It is of great interest to study the cause of the intrinsic rhythmicity. The authors suggest the intriguing possibility that the pacemaker cells contain more sodium and less potassium than the nonpacemaker cells. In such cells the level of E_K would be shifted in the direction of depolarization. An increase in permeability to K (P_K) associated with repolarization would bring the transmembrane potential close to E_K. The subsequent decrease in P_K to the level characteristic of phase 4 would permit the ionic currents carried by Na or other ions to progressively lower the membrane potential and thereby provide depolarization during phase 4.

In the chapter on the atrioventricular node the authors study the mechanism of delay. Erlanger pointed out the possibility that the delay occurs as the result of a latency at the transition zone between atrial fibers and fibers of the atrioventricular node.

In the chapter on Purkinje fibers it is interesting to note that the authors believe that the U wave is merely the surface record of repolarization of the ventricular Purkinje system, that is, the U wave is the Purkinje fiber T wave. Two arguments favor this: potassium produces marked variations in the U wave and a marked effect on phase 3 or Purkinje potential. In addition, the potential of Purkinje fibers is considerably longer than that of ventricular muscle and the phase of rapid repolarization of Purkinje fibers is coincident in time with the U wave.

In chapter 8, excitability is studied and the authors establish a clear difference between cathodal and anodal stimulation. Four new concepts of the greatest importance are presented: (1) regenerative repolarization, (2) all or none repolarization, (3) propagated repolarization and (4) break reexcitation. It seems likely, as the authors state, that propagation of repolarization exists in the normal heart. Since repolarization propagates very slowly (about 0.2 mm./sec.) one would not expect a single pacemaker. Each area which repolarizes before an adjoining area would then contribute to the repolarization of the adjoining area. Therefore, repolarization would be a propagated process with multiple foci of origin.

The last chapter is a general revision of the electrophysiology of the heart and is fundamental for every cardiologist and electrocardiologist. As a particular example, one could choose the section on the possible mechanism of repolarization.

Anyone who is interested in obtaining a basic understanding of the intrinsic mechanism of electrocardiology and electrophysiology can do so by studying the principles as set forth in this excellent book.

DEMETRIO SODI-PALLARES, M.D.

Angiocardiopneumographie Élargie: Méthode D'Opacification Vasculaire Générale par Voie Veneuse, by P. Viallet, L. Sendra, L. Chevot, P. Aubry and P. Combe. Masson & Cie, Paris, 1959, pp.110, 4,400 fr.

As a rule, opacification of the circulatory system is effected by the venous route. In order to avoid delays in injection, the authors insist on the need for as large a tube as possible from the injection syringe to the venous cannula and on the desirability of a massive flow of physiologic saline solution at the end of the injection to force the contrast medium to the right side of the heart. During the left heart phase, large roentgenograms record opacification of large areas. The method is, therefore, classic.

Thanks to the atlas-type format of the book and the use of excellent paper, the authors have been able to include a number of fairly large angiocardiograms of good quality reproduction.

The text is extremely concise.

R. HEIM DE BALSAC, M.D.

Mitral Valvulotomy, by Harold J. Stewart and Frank Glenn. Charles C Thomas, Springfield, Ill., 1959, pp. 244, $10.50.

This publication is a critical review of the first 300 patients operated upon at the New York Hospital-Cornell Medical Center from 1951 to 1956. It is divided into three complete sections although some effort at correlation and integration has been made. The first section presents the selection and management of the first 100 patients treated surgically (1951–1953). A brief, outlined discussion of this selection, the preoperative work-up, operative technic and postoperative care are included. These patients were evaluated with great care and the results obtained have been recorded with equal care. Section II is a similar type of analysis of the second and third 100 patients in which the same general criteria of evaluation and management were used but somewhat modified in the light of experience obtained from the first 100 consecutive patients. Section III is a long-term evaluation of the first 100 patients having undergone mitral valvular surgery and presents detailed data of results, complications encountered and an analysis of deaths. A comprehensive bibliography which includes references from most of the investigators in this field is appended.

It is believed that this volume contains the carefully evaluated experience of a well controlled and investigated series of patients with mitral stenosis and is worthwhile reading for those interested in the proper selection of patients for mitral valvulotomy. Although somewhat disjointed in style and perhaps repetitive it presents a comprehensive evaluation of a statistically significant number of cases. No attempt has been made to give a detailed discussion of all the problems involved in the selection of such patients for surgery. The pathology of the valve itself and the details of the technic of surgical management are not included in the discussion to any practical degree. The results obtained in the entire series would indicate that when subjected to careful preoperative management and selection the patient suffering from significant mitral stenosis will receive both immediate and long-term benefit from properly performed valvulotomy.

For those primarily interested in learning the practical basic criteria for the selection of patients for mitral valvular surgery this monograph is recommended.

ROBERT P. GLOVER, M.D.

Current Therapy—1960. Latest Approved Methods of Treatment for the Practicing Physician, edited by Howard F. Conn. W. B. Saunders Co., Philadelphia, 1960, pp. 808, $12.00.

In this latest edition of *Current Therapy*, under the able editorship of Dr. Howard F. Conn, the section on the cardiovascular system includes articles on diseases of the aorta, cardiac arrhythmias, angina pectoris, bacterial endocarditis, heart failure, hypertension, congenital lesions and peripheral arterial and venous diseases. Most of the therapeutic summaries are brief and to the point. Of particular interest are Brill's and Hurst's reviews of the treatment of atrial fibrillation and paroxysmal tachycardia, Moyer and Brest's regimen for hypertension and hypertensive crises and Hellerstein's excellent summary of the management of myocardial infarction.

S. D.

Der Arbeits- und Trainingseinfluss auf Kreislauf und Atmung, by W. Hollman, Dr. Dietrich Steinkopff Verlag, Stuttgart, 1959, pp. 202, DM 37.50.

Hollmann's book on *The Influence of Exercise and Training upon Circulation and Respiration* is a timely and enlightening contribution to one of the most pressing problems in our age of physical inactivity. Due to his dual position both in Professor Knipping's Medical Clinic, a renowned center of exercise research, and in the Sporthochschule in Cologne, the author commands an unusual range of theoretic knowledge and practical experience in the field of cardiology as well as sports medicine. Owing to the "economic miracle" of postwar Germany, motorization and automation are claiming cardiac victims there in staggering numbers (80,000 in 1950 and 183,000 in 1952), contradicting the old notion that life-long exercising "wears out the heart."

The author presents an excellent survey of the fundamentals of dynamic, metabolic and neuroregulatory cardiovascular and respiratory physiology in relation to physical exercise and training. Data are largely based on personal investigations and on the extensive studies of German workers over the last two decades.

Functional and morphologic characteristics of the trained heart are discussed in detail, and its superior qualities are emphasized, including "regulatory" dilatation whose misleading appearance on the x-ray screen has contributed so much to the traditional fear of "athlete's heart" as an allegedly pathologic phenomenon. Great significance is being attributed to neurovegetative (vagal) influences in establishing the training-induced dynamic qualities and energetic efficiency of the heart muscle. Reactions of the blood pressure to training were found less impressive.

Overtraining, especially in juvenile persons, is warned against. On the other hand, continued adequate training to a practically unlimited old age is recommended as not only possible but also as highly beneficial, in compliance with the principle: "inactivity weakens, excessive activity injures, adequate activity strengthens the heart." Accordingly, practical rules for the adjustment of training to cardiac tolerance and specific contraindications are outlined.

Credit is given to the pioneering rehabilitative exercise practices as applied in the U.S.A. in outright pathologic persons. The prophylactic value of systematic exercising, particularly in sedentary persons with cardiovascular neurovegetative dysregulation and sympathetic overactivity, is stressed in view of the rapidly increasing early cardiovascular invalidism among the German people. (In this country, no systematic attempts at preventive mass reconditioning have yet been undertaken.)

Hollmann's style is clear and concise, instructive graphs and illustrations are plentiful and the book has a great deal of useful and novel information to offer to American physicians, physiologists and physical educators. An English translation would be desirable to strengthen the awareness in this country of the importance of exercising for the preservation of cardiac health. W. RAAB, M.D.

RECEIVED FOR REVIEW

Hypertension. Volume VIII. Renal, Electrolyte and Autonomic Factors, edited by Floyd E. Shelton. American Heart Association, Inc., New York, 1960, pp. 150.

Chemistry of Heart Failure, by William C. Holland and Richard L. Klein. Charles C Thomas, Springfield, 1960, pp. 116, $5.50.

Cardiac Emergencies and Related Disorders, by Harold D. Levine. Landsberger Medical Books, Inc., New York, 1960, pp. 381, $12.00.

Differential Diagnosis of the Electrocardiogram, by Sidney R. Arbeit, Ira L. Rubin and Harry Gross. F. A. Davis Company, Philadelphia, 1960, pp. 212, $10.50.

Psychiatry in the Medical Specialties, by Flanders Dunbar. McGraw-Hill Book Company, Inc., New York, 1960, pp. 535, $12.00.

Treatment of Cardiovascular Emergencies, by Aldo A. Luisada and Leslie M. Rosa. McGraw-Hill Book Company, Inc., New York, 1960, pp. 122, $4.95.

Embolic Dispersoids in Health and Disease, by Gus Schreiber. Charles C Thomas, Springfield, 1960, pp. 85, $5.50.

Fundamentals of Chest Roentgenology, by Benjamin Felson. W. B. Saunders Co., Philadelphia, 1960, pp. 301.

Medical Problems of Modern Air Travel, by Harold V. Ellingson. F. A. Davis Company, Philadelphia, 1960, pp. 26.

Blood Flow in Arteries, by Donald A. McDonald. Williams & Wilkins Company, Baltimore, 1960, pp. 328, $8.50.

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Diseases of the Newborn, by Alexander J. Schaffer and Milton Markowitz. W. B. Saunders Co., Philadelphia, 1960, pp. 878.

Congenital Heart Disease. A Symposium at the Washington Meeting of American Association for Advancement of Science. December 29–30, 1958, by A. D. Bass and G. K. Moe. American Association for the Advancement of Science, Washington, D. C., 1960, pp. 364, $7.50.

Cinefluorography, edited by G. H. S. Ramsey, J. S. Watson, Jr., T. A. Tristan, S. Weinberg and W. S. Cornwall. Charles C Thomas, Springfield, 1960, pp. 266, $11.75.

Electron Microscopy of the Cardiovascular System, by Bruno Kisch. Charles C Thomas, Springfield, 1960, pp. 180, $7.50.

Transactions. Volume VI. American Society for Artificial Internal Organs, edited by George E. Schreiner. Georgetown University Press, Washington, D. C., 1960, pp. 380, $8.00

College News

President's Column

Admission Requirements of the American College of Cardiology

It is my privilege to fulfil a request by President Louis Bishop to discuss the philosophy and practical aspects relative to requirements for membership in the American College of Cardiology. This of necessity involves comments relative to the aims of the College and the activities of the Credentials Committee.

In brief, the aims of the College are the formation of a fellowship for coordinated educational and creative activities of men and women with special interests, training and qualifications in cardiology, be they internists, pediatricians, surgeons, radiologists or basic scientists. These individuals must have not only a significant interest in cardiology but also would be expected to invest the major portion of their professional activities in cardiovascular matters. The College has no interest in being a certifying body, but rather the diploma of the College is only awarded to a Fellow of the College as recognition of achievement as a person who has fulfilled the qualifications, productivity and usefulness of a true cardiologist in his special field of endeavor.

The mechanism for admission to the College involves a detailed review of a candidate's qualifications by the Credentials Committee, whose recommendations are then submitted to the Board of Trustees for final approval. As the College has developed into a fellowship of truly or potentially qualified cardiologists, the requirements for admission have become increasingly stringent and specific, especially so in regard to younger men. There are three basic grades to which an applicant may be elected. Diplomas are awarded only to those men attaining the status of full fellowship.

Membership: Fundamentally the status of Membership constitutes a basic candidate group. These men are in their late twenties or the thirties. They have completed an accredited residency training in internal medicine, pediatrics or general surgery. In addition to this they have either completed or are in the process of obtaining additional training in (1) medical or pediatric cardiology, or (2) thoracic and cardiovascular surgery. Of such is the future structure and growth of the College. Within five years after election to Membership these men must (1) demonstrate growth and development in cardiology and (2) complete their basic board certification in Internal Medicine, Pediatrics or Thoracic Surgery. They are then eligible for advancement to Associate Fellowship. Failure to progress in this manner within the five year period results in withdrawal from the College.

Associate Fellowship: The grade of Associate Fellow is awarded to successful candidates from the Membership group or may be given directly to qualified applicants. Such qualifications involve adequate basic residency training, specialized cardiologic training and completion of either the Board of Internal Medicine, Pediatrics or of Thoracic Surgery. The stringency of these requirements relative to board certification are rigidly upheld for all candidates under forty-three years as of this date, but this age level increases one year with each passing year (i.e., forty-four years in 1961, forty-five years in 1962, etc.). For a man over forty-three years to be admitted without board certification, he must present evidence of a significant amount of cardiologically oriented publications, institutional connections, and other indications that he is a "senior citizen" in cardiology. An Associate Fellow is allowed seven years in which to fulfil requirements for advancement to Full Fellowship.

Fellowship: The requirements for promotion to, or direct admission as, a Full Fellow involve (1) certification by the board in his basic discipline (internal medicine, pediatrics, thoracic surgery or radiology), (2) evidence of con-

tinued and progressive activity in cardiology so that he could be either reasonably considered for certification by the Subboard of Cardiovascular Disease, or be so certified (i.e., candidates involved in medical or pediatric cardiology). Thoracic surgeons or radiologists must demonstrate major interests and activities in cardiovascular disease.

These then are the requirements for admission to specific grades for applicants from the United States. Applicants from Canada must receive approval of the Canadian member of the Credentials Committee, fulfil the requirements specified above and, in addition, must have achieved the M.R.C.P. (Canada) for Associate Fellowship, or the F.R.C.P. (Canada) for Full Fellowship. Candidates from England may achieve Full Fellowship with adequate qualifications plus the M.R.C.P. (England) since the F.R.C.P. (England) is not achieved by examinations but is a later honorary recognition of achievement. Candidates from Mexico have equally stringent qualifications and must receive approval of the Mexican representative on the Credentials Committee. Fellowships are occasionally granted to outstanding cardiologists in other countries.

Credentials Committee: The Credentials Committee itself consists of three Fellows of the College, two of whom are medical cardiologists and the other a cardiovascular surgeon. A single ex-officio member from both Canada and Mexico is involved relative solely to applicants from his individual country. The committee reviews the qualifications of the candidate, the letters from two sponsors who are Fellows of the College other than the local Area Governor, plus the Governor's findings and recommendations. The Governor in each individual instance is required (1) to conduct a rather exhaustive inquiry into the standing of the candidate in his local community, (2) to contact reputable Fellows of the College intimately connected with the applicant, and (3) wherever possible to interview personally the candidate or arrange for the same by an adequate deputy.

It should be emphasized that the Credentials Committee is a screening and advisory group, deeply cognizant of the responsibility placed upon it in regard to the future growth of the College in quality and stature. Its deliberations and actions require time and rarely can it reach a final recommendation in less than three months from the time of the candidate's initial application. During this interval, the College office must confirm the applicant's qualifications, obtain a detailed report from the local Area Governor, receive all needed sponsorship letters and allow the Committee members to tap all necessary sources of information relative to the applicant before final deliberations and recommendations. The final word relative to action upon any candidate's acceptance rests with the Board of Trustees. In a similar manner the dropping of men from the College who do not fulfil the required advancement in grade specified in the by-laws (five years from Membership to Associate Fellowship, seven years from Associate Fellowship to Full Fellowship) is a matter for final action by the Board of Trustees.

The Credentials Committee and the Board of Trustees are strongly in favor of the activities and usefulness of the Subboard of Cardiovascular Disease. They have become progressively stringent in their requirement that all younger cardiologists must achieve this certificate of achievement before advancement to, or direct admission as, a Full Fellow of the American College of Cardiology.

Finally, the writer (who has had the privilege of being Chairman of the Credentials Committee for the past three years) wishes to express his appreciation to the Governors and to past members of this committee. He especially wishes to commend the members of this year's committee, namely, Dr. E. Grey Dimond (President-Elect of the College), Dr. George R. Herrmann (Honorary Fellow), Dr. G. W. Manning, representative for Canada, and Dr. Demetrio Sodi-Pallares, representative for Mexico.

OSLER A. ABBOTT, M.D., F.A.C.C.
Past President of the College
Chairman, Credentials Committee

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Recommended Daily Dietary Allowances and the Nutritional Contribution of a Basic Cereal and Milk Moderate Low-Fat Breakfast*

Menu: Orange Juice—4 oz.;
Cereal, dry weight—1 oz.;
Whole Milk—4 oz.; Sugar—1 teaspoon;
Toast (white, enriched)—2 slices;
Butter—5 gm. (about 1 teaspoon);
Nonfat Milk—8 oz.

Nutrients	Calories	Protein	Calcium	Iron	Vitamin A	Thiamine	Riboflavin	Niacin equiv.	Ascorbic Acid
Totals supplied by Basic Breakfast	503	20.9 gm.	0.532 gm.	2.7 mg.	588 I.U.	0.46 mg.	0.80 mg.	7.36 mg.	65.5 mg.
Recommended Dietary Allowances—Women, 65 Years (58 kg.—128 lb.)	1800	58 gm.	0.8 gm.	12 mg.	5000 I.U.	1.0 mg.	1.5 mg.	17 mg.	70 mg.
Percentage Contributed by Basic Breakfast	27.9%	36.0%	66.5%	22.5%	11.8%	46.0%	53.3%	43.3%	93.6%

Cereal Institute, Inc.: Breakfast Source Book. Chicago: Cereal Institute, Inc., 1959.
Food & Nutrition Bd.: Recommended Dietary Allowances, Revised 1958. Natl. Acad. Sci.—Natl. Research Council Publication 589, 1958.
Watt, B. K., and Merrill, A. L.: Composition of Foods—Raw, Processed, Prepared. U.S.D.A. Agriculture Handbook No. 8, 1950.

**The allowance levels are intended to cover individual variations among most normal persons as they live in the United States under usual environmental stresses. Calorie allowances apply to individuals usually engaged in moderate physical activity. For office workers or others in sedentary occupations they are excessive. Adjustments must be made for variations in body size, age, physical activity, and environmental temperature.*

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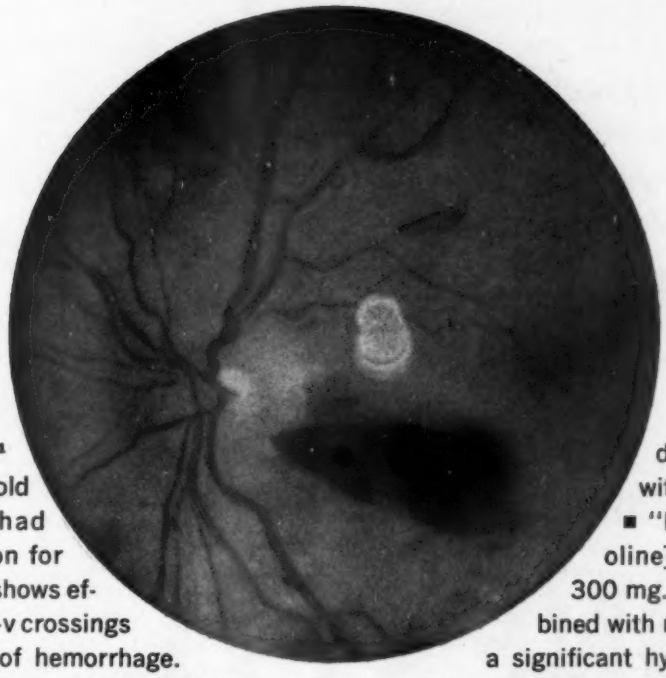

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1. Bedell, A. J.: Clin. Symposia 9:135 (Sept.-Oct.) 1957.
2. Lee, R. E., Seligman, A. M., Goebel, D., Fulton, L. A., and Clark, M. A.: Ann. Int. Med. 44:456 (March) 1956.

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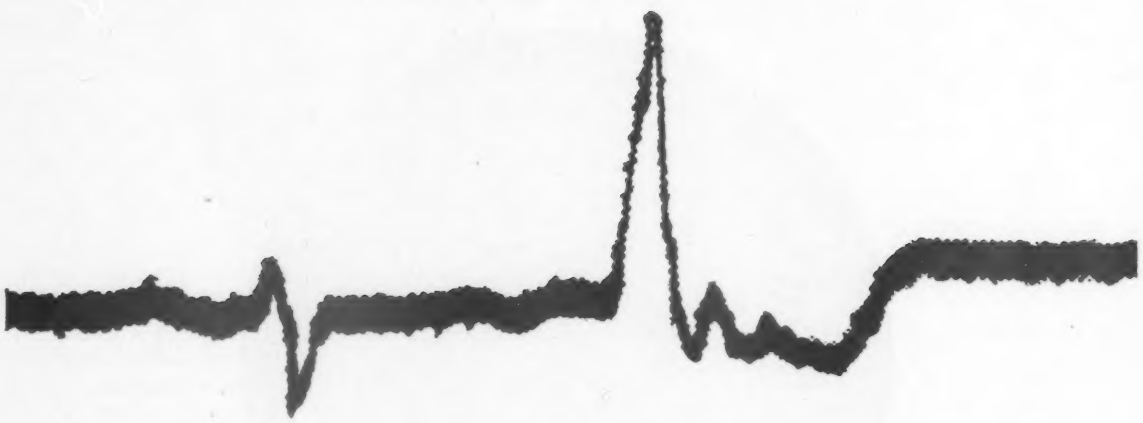

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References: 1. Zapata-Diaz, J., et al.: Am. Heart J. 43:854, 1952. 2. Modell, W.: In Drugs of Choice, C.V. Mosby Co., St. Louis, 1958, p. 454. 3. Kayden, H. J., et al.: Mod. Concepts Cardiovasc. Dis. 20:100. 1951. 4. Miller, H., et al.: J.A.M.A. 146:1004, 1951.

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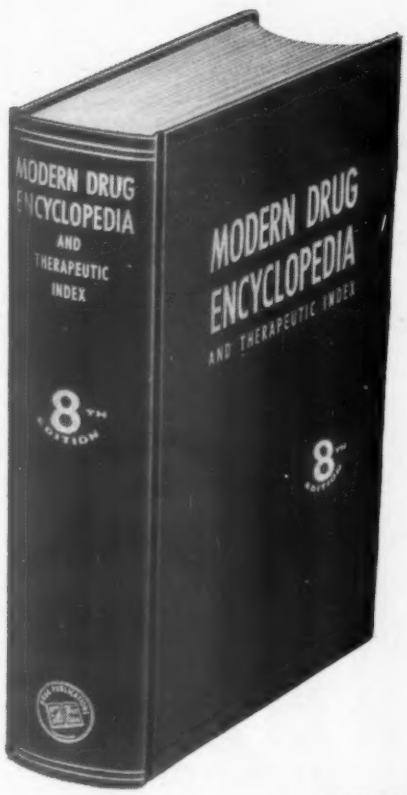
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1. Baer, S., et al.: J.A.M.A. 167:704, June 7, 1958. 2. Moser, K. M.: Disease-a-Month, Chicago, Yr. Bk. Pub., Mar., 1960, p. 13.

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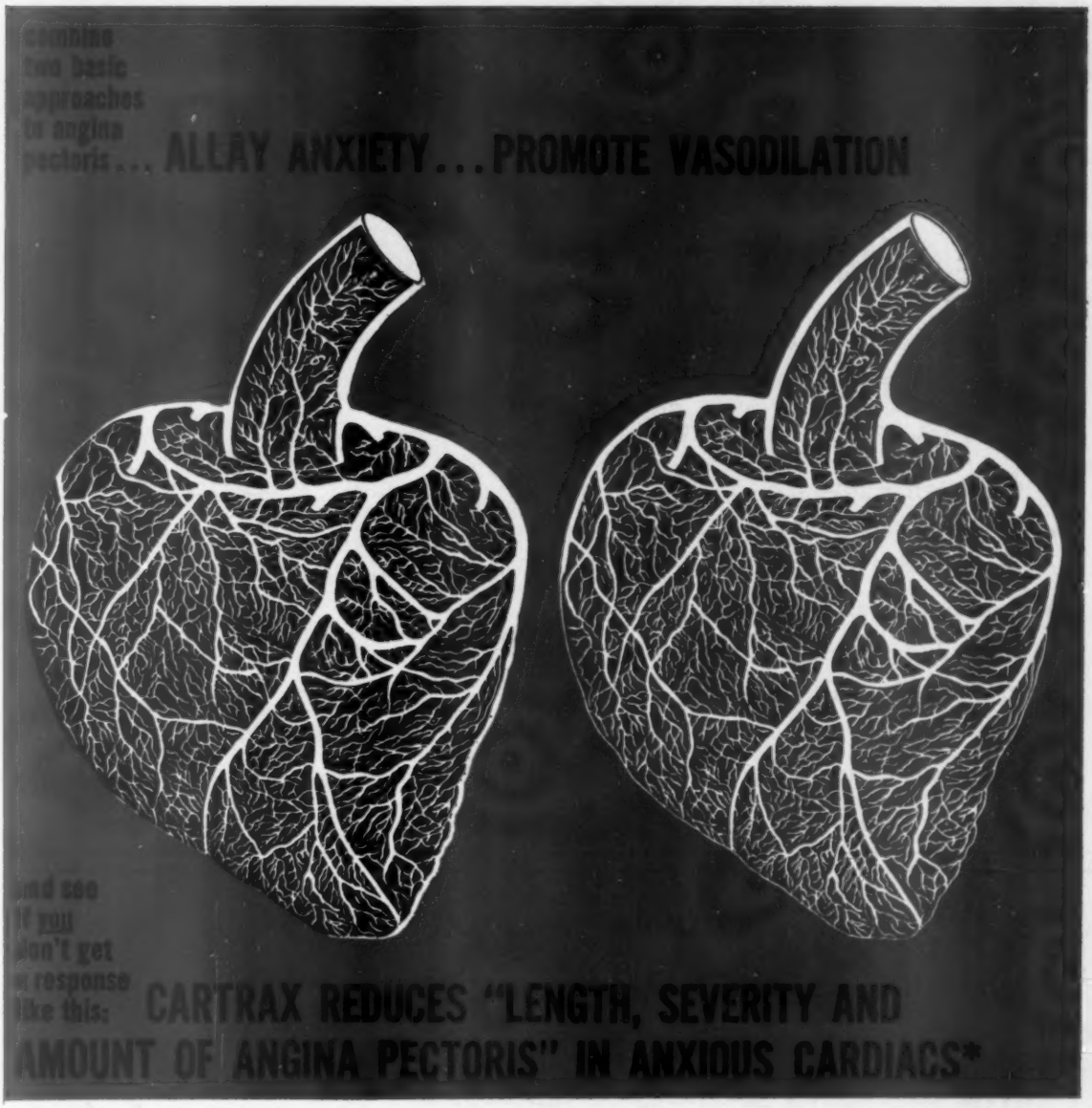

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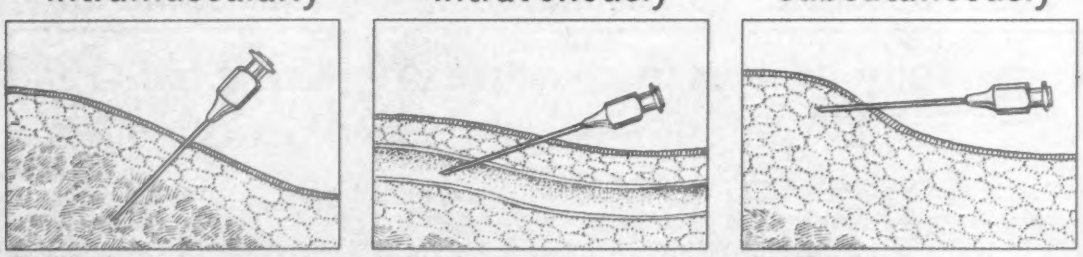

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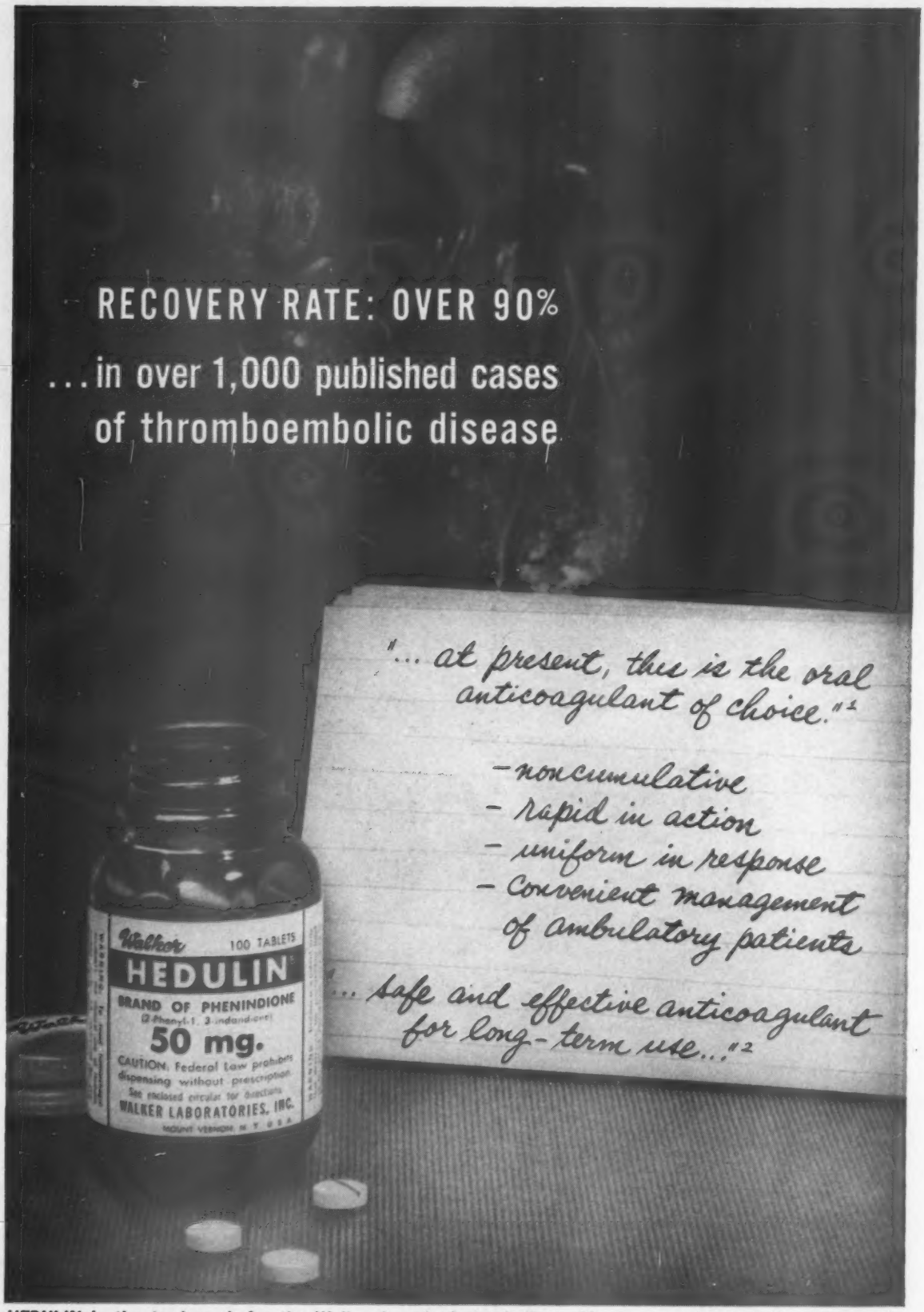
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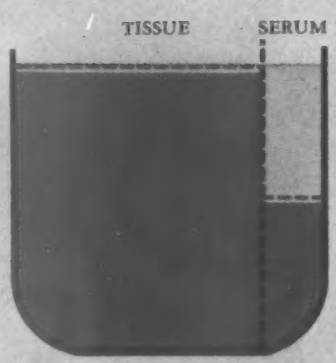

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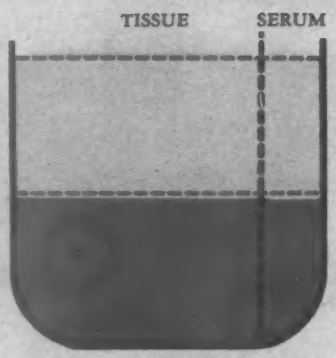

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*U. S. Patent 2,895,881

1. Greif, E and Scheuer, J.: J Mount Sinai Hosp., Nov./Dec. 1960

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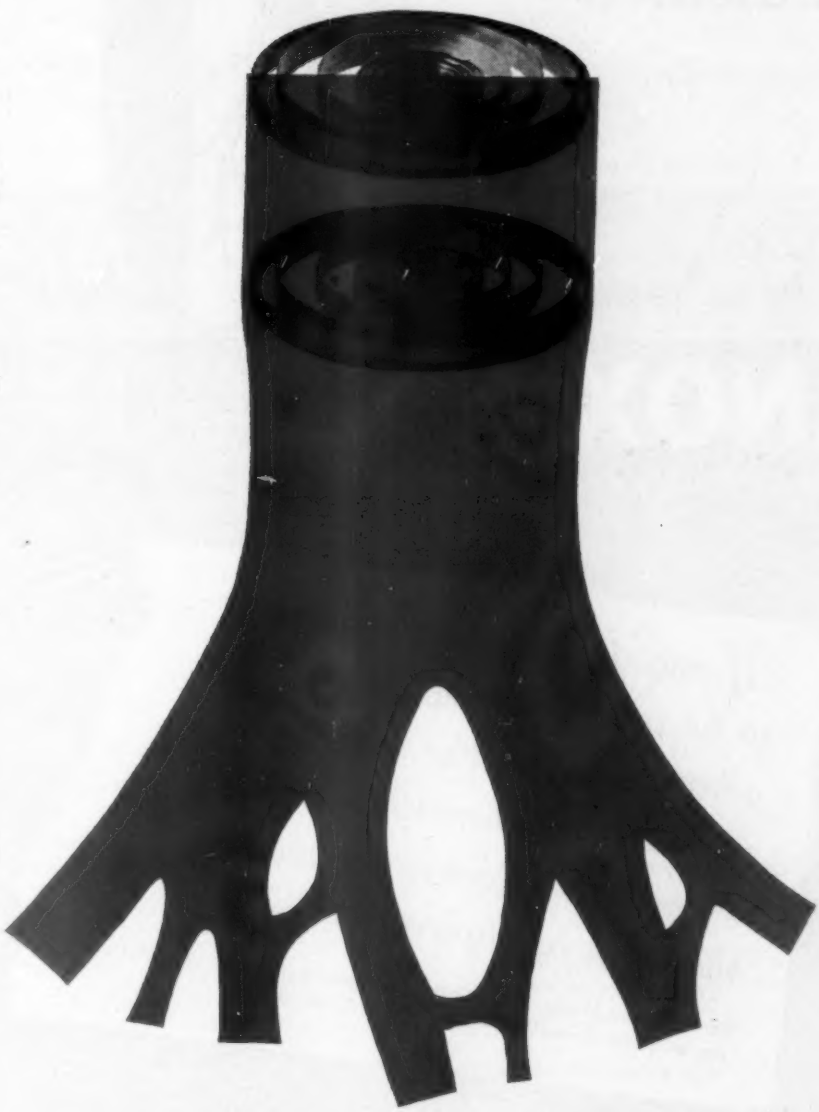

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References: 1. Ford, R. V.: Current Therap. Research 2:347, 1960. 2. Fuchs, M., and others: Current Therap. Research 2:11, 1960. 3. Ford, R. V.: Connecticut Med. 24:704-707, (Nov.) 1960. 4. Ford, R. V.: Texas State J. Med. 56:343, 1960.

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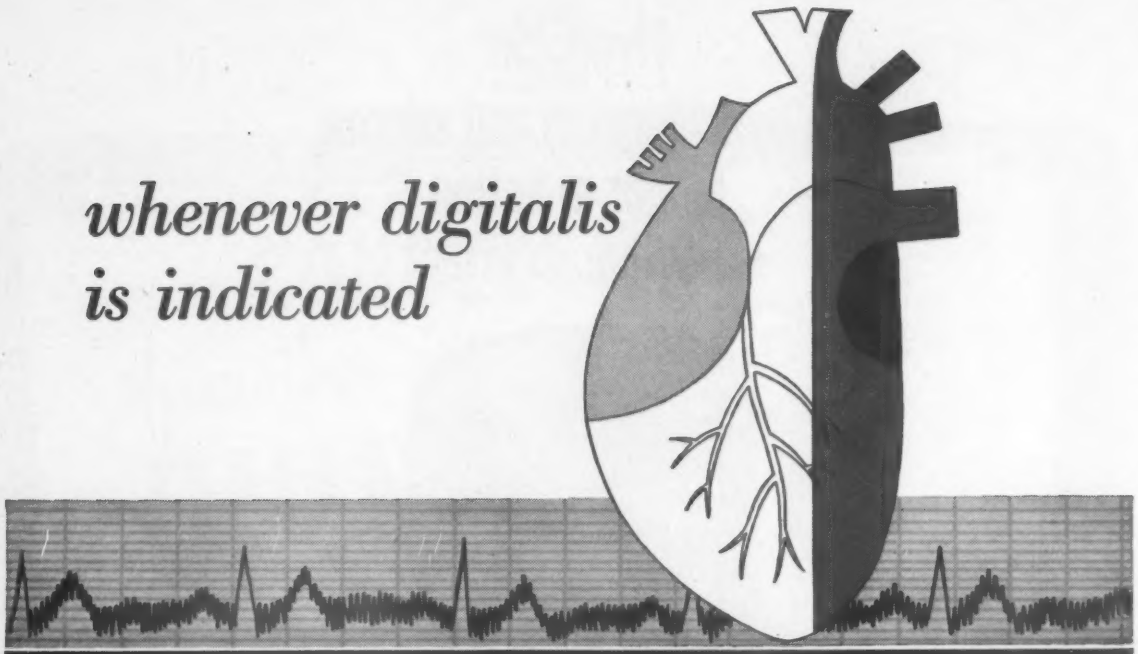

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Cardiovascular patients respond in a few days. Thanks to your prompt treatment and the smooth action of Deprol, his depression is relieved and his anxiety calmed – *often in two or three days.* He eats well, sleeps well and his depression no longer complicates your basic regimen.

Lifts depression...as it calms anxiety!

For cardiovascular patients–a smooth, balanced action that lifts depression as it calms anxiety...rapidly and safely

Balances the mood–no "seesaw" effect of amphetamine-barbiturates and energizers. While amphetamines and energizers may stimulate the patient – *they often aggravate anxiety and tension.* And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression.*

In contrast to such "seesaw" effects, Deprol lifts depression as it calms anxiety – both at the same time.

Acts swiftly–the patient often feels better, sleeps better, within two or three days. Unlike most other antidepressant drugs, Deprol relieves the patient quickly – often within two or three days.

Acts safely – no danger of hypotension. Deprol does not cause hypotension, tachycardia, jitteriness, or liver toxicity. It can be safely administered with basic cardiovascular therapy.

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be gradually increased up to 3 tablets q.i.d.
Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.
Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

Deprol

WALLACE LABORATORIES
Cranbury, N. J.

58-765

Pacemaker Model TR-3 shown ⅔ actual size.

NEW MINIATURE CARDIAC PACEMAKER

BATTERY POWERED, ALL-TRANSISTOR CARDIAC PACEMAKER . . . READY FOR INSTANTANEOUS STIMULATION AT ALL TIMES

Another proven ELECTRODYNE instrument developed in conjunction with Paul M. Zoll, M. D. is now available. The all-transistor Pacemaker represents an important addition to the highly specialized line of proven cardiac life-saving instruments now offered by ELECTRODYNE. No time loss, just flip the switch and within three seconds the new TR-3 is delivering stimulation. Operates from one long-life battery or, as an additional feature, may be plugged into any standard AC outlet.

The TR-3 provides the necessary currents for both external and direct stimulation of the heart through completely independent outlets and cord sets. The amplitude of the stimulus is continuously variable from 0-150 volts for external stimulation and 0-15 volts for direct stimulation.

A built-in compartment holds complete accessories easily available for immediate action.

Open heart surgery: Provision for direct stimulation of heart for treatment of post-operative heart block through a wire attached directly to the myocardium.

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If postcoronary management is of special interest to you, consider the demonstrated value of sublingual heparin . . .

"In a controlled clinical study of 260 postcoronary patients, one-half were given sublingual heparin and one-half received conventional treatment. During the period of observation, averaging more than 2 years per patient, there were 12 recurrent infarctions in the heparin-treated group and 38 in the control group. This difference is statistically significant."

Fuller, H. L.: Angiology *11*:200 (June) 1960.

Simple and safe for long-term therapy, Clarin* (sublingual heparin) effectively controls the prolonged postprandial lipemia associated with atherosclerosis by facilitating the normal physiologic breakdown of fats. Unlike parenteral heparin, the use of Clarin requires no clotting-time or prothrombin determinations. The antilipemic activity of each manufactured lot of tablets is confirmed by sublingual control tests in animals.

Indication: For the management of hyperlipemia associated with atherosclerosis, especially in the postcoronary patient. *Dosage:* After each meal, hold one tablet under the tongue until dissolved. *Supplied:* Bottles of 50 pink, sublingual tablets, each containing 1500 I.U. heparin potassium.

An informative booklet, "Hyperlipemia, Heparin and Management of the Postcoronary Patient," is available from Thos. Leeming & Co., Inc., 155 East 44th St., New York 17, N. Y.

*Registered trade mark. Patent applied for.

Clarin

(sublingual heparin potassium, Leeming)

JAN 24 1962
DEC 29 1954
MAY 18 1961
DEC 12 '61
SEP 21 '61
APR 23 1962
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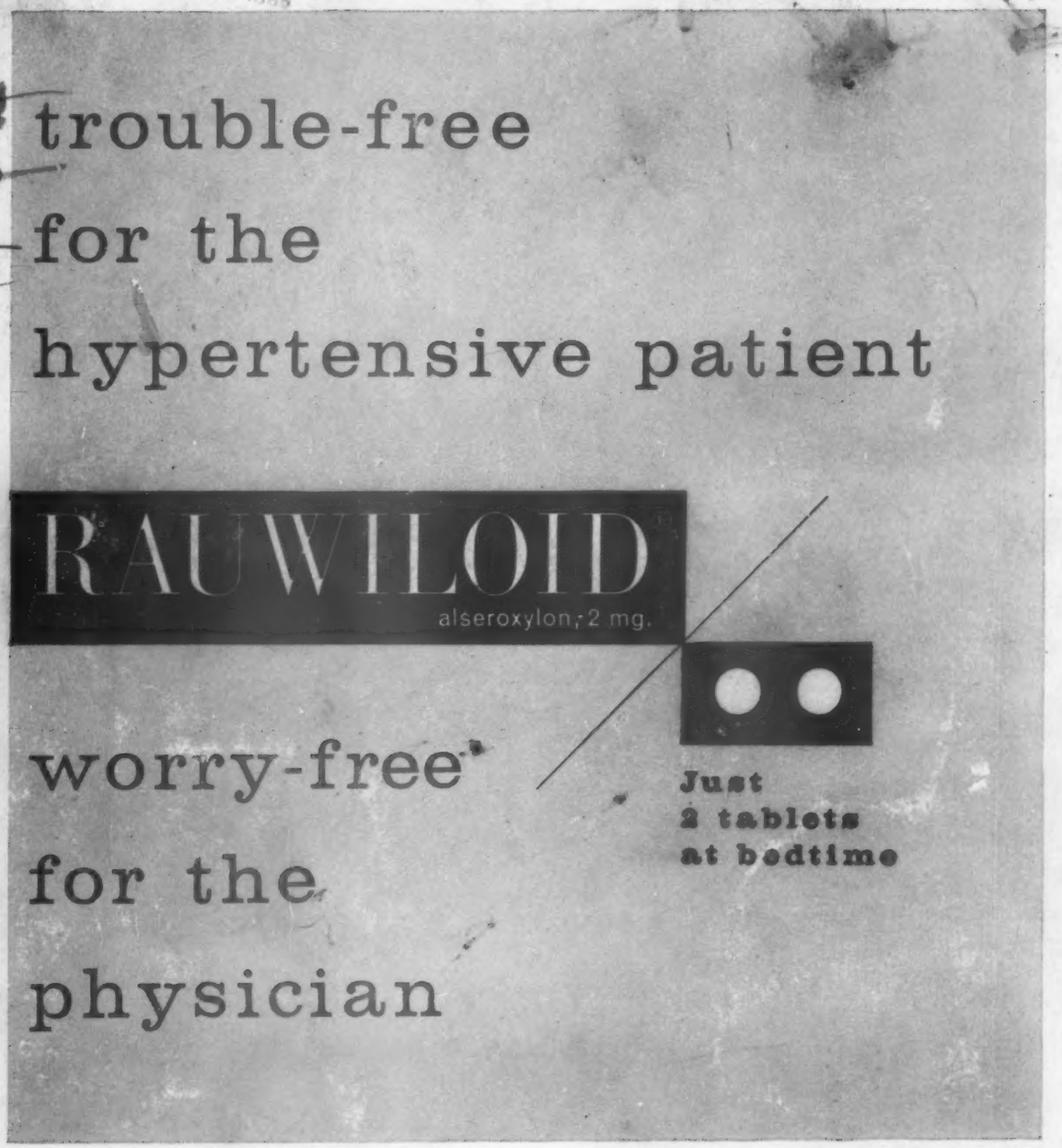
APR 5 1965
SEP 15 1966



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